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NITROGEN MUSTARD THERAPY IN CUTANEOUS BLASTOMATOUS DISEASE

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The paucity of reports in the literature on the use of nitrogen mustard therapy in cutaneous blastomatous disease leads us to report our experiences in the treatment of 4 patients in this category and 1 additional patient presenting a widespread inflammatory dermatosis. The series includes 2 cases of mycosis fungoides, 1 of lymphosarcoma involving the skin, 1 of Kaposi's hemorrhagic sarcoma associated with Hodgkin's disease and 1 of chronic disseminated lupus erythematosus.

Gilman and Philips [1] in April 1946 reported a large number of scientific investigations on the biologic actions and therapeutic applications of beta-chloroethyl amines and sulfides. Within a few months, three clinical papers [2] appeared on the use of beta-chloroethyl amines, known as nitrogen mustards, in the treatment of certain neoplastic diseases, particularly Hodgkin's disease, lymphosarcoma, leukemias and certain related tumors. Only in April 1947, in the *Journal of Investigative Drmatology,* was there a report by Henstell and Tober [3] on the use of nitrogen mustards in the treatment of 1 case of mycosis fungoides. The patient responded favorably, but no follow-up was reported.

In view of the recent publications cited, we wish only to summarize in this article the high points in the development of nitrogen mustards for clinical use. During World War II, studies were made in an attempt to develop satisfactory methods to combat the irritating effects of mustard gas (bis[2-chloroethyl] sulfide). A number of nitrogenous analogues were also studied. These compounds were called nitrogen mustards. It was found that the sulfur and nitrogen mustards not only were contact vesicants but after absorption brought about cytotoxic actions on a variety of tissues. Cellular susceptibility to the compounds was related in a general way to the degree of proliferative activity of the cells. This action was different from that of any other known chemical agent and it resembled in some respects the effect of roentgen rays on cells. It was found that in normal tissues the most susceptible were those of the blood-forming organs and the lining of the gastrointestinal tract. In both animals and human beings the drugs produced lymphopenia, granulocytopenia, thrombopenia and varying degrees of anemia. The severity of this response was in direct relationship to the dosage employed. Larger doses produced almost complete aplasia of the bone marrow and lymphatic atrophy and also swelling and necrosis of the lining of the gastrointestinal tract. Threshold doses affected cells in which there was mitotic activity at the time of exposure. Nuclear fragmentation was also produced. This change was noted in the cells of many plants as well as animals. Experiments on transplanted lymphosarcoma in mice revealed that dissolution of the tumor could be rapidly effected with doses bordering on the toxic. These tumors invariably returned.

The decided effect of nitrogen mustards on lymphoid tissue led to the experimental use of these compounds in the treatment of various types of lymphomas. Briefly, the clinical papers referred to in a foregoing paragraph agree that these compounds are most valuable in the treatment of Hodgkin's disease and lymphosarcoma. In the former, regression of the lymph nodes and decrease in the size of the liver and spleen, with remissions lasting four to eight months, have been frequent. The cutaneous lesions of Hodgkin's disease may or may not be affected, and pruritus is slightly and inconstantly relieved. The effects of the treatment seemed to be similar to those observed following roentgen treatment. In cases of widespread Hodgkin's disease, when it was impractical to give roentgen treatment over large areas, nitrogen mustard compounds have been found particularly useful in bringing about remissions. Also in patients with Hodgkin's disease and lymphosarcoma whose disease had become resistant to further radiation the use of these compounds brought about remission. This has led to the hope that these diseases, once resistant to further radiation, might again become sensitive to this form of therapy after the use of nitrogen mustards. It has been strongly pointed out that the use of these compounds does not cure; it is rather a symptomatic palliative method of treatment. Previous authors have emphasized that the margin of safety in the use of these chemicals is narrow and that one must use them with extreme caution. The blood cell count must be carefully watched at frequent intervals as a

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These studies and reports are from the Edward J. Meyer Memorial Hospital and the Buffalo General Hospital units in the University of Buffalo School of Medicine. Nitrogen mustard therapy was given only on the approval of the Tumor Committee of each institution. The administration of the treatment and medical care was under the supervision of the medical department in each hospital.

1. Gilman, A., and Philips, F. S.: The Biological Actions and Therapeutic Applications of the B-Chloroethyl Amines and Sulfides, Science **103**: 409-415 (April 5) 1946.

2. Rhoads, C. P.: Nitrogen Mustards in the Treatment of Neoplastic Diseases, J. A. M. A. **131**: 656-658 (June 22) 1946. Goodman, L. S.; Wintrobe, M. M.; Dameshek, W.; Goodman, M. J.; Gilman, A., and McLennan, M. T.: Clinical Experience Through the Use of Methyl-bis (Beta-Chloroethyl) Amine Hydrochloride and Tris (Beta-Chloroethyl) Amine Hydrochloride (Nitrogen Mustards) in the Therapy of Hodgkin's Disease, Lymphosarcoma, Leukemia, and Certain Allied Miscellaneous Disorders, ibid. **132**: 126-132 (Sept. 21) 1946. Jacobson, L. O.; Spurr, C. L.; Barron, E. S. G.; Smith, T.; Lushbaugh, C., and Dick, G. F: Nitrogen Mustard Therapy, ibid. **132**: 263-271 (Oct. 5) 1946.

3. Henstell, H. H., and Tober, J. N.: Treatment of Mycosis Fungoides with Nitrogen Mustard, J. Invest. Dermat. **8**: 183-188 (April) 1947.

guide to continued treatment. Serious late toxic effects can be largely prevented by adherence to safe dosage schedules.

From the clinical standpoint, studies on the use of only two compounds have been reported to date, namely; methyl-bis(beta-chloroethyl)amine and tris

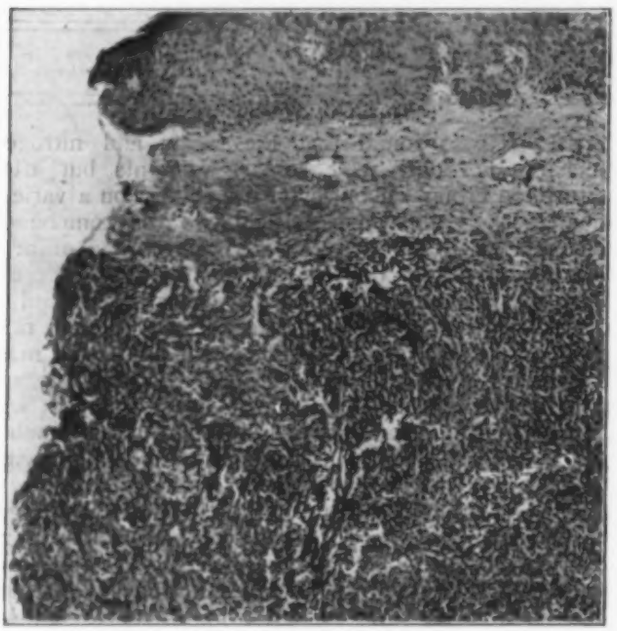

Fig. 1 (case 1).—Section of tumor showing infiltrate of mycosis fungoides before treatment with nitrogen mustard. Hematoxylin and eosin; × 75.

(beta-chloroethyl)amine hydrochloride. The usual doses employed have been 0.1 mg. per kilogram of body weight administered intravenously on four successive days, making a total dose of 0.4 mg. per kilogram. This has frequently caused nausea, vomiting and diarrhea, as well as effects on the blood-forming organs, which manifest themselves in the peripheral blood by leukopenia, normocytic anemia and thrombopenia. If these changes are pronounced, bleeding from the gums and purpuric lesions of the skin occur. The total leukocyte count declines progressively for fifteen to twenty-five days and returns to normal, usually within two weeks after the maximum reduction.

Because of the close cytologic relationship between Hodgkin's disease, lymphosarcoma, leukemia and mycosis fungoides, we felt that the latter disease should be equally favorably affected by the use of nitrogen mustard compounds. Two patients presenting rapidly advancing cases of mycosis fungoides soon presented themselves for treatment.

The nitrogen mustard used in the treatment of our patients was methyl-bis(beta-chloroethyl)amine hydrochloride.

REPORT OF CASES

Case 1.—The diagnosis was mycosis fungoides. Mrs. G. S., a white woman aged 54, gave a history of a rash beginnning on the face in May 1944, following a severe sunburn. This rash spread to involve most of the body, accompanied with severe itching. Under treatment by various physicians the condition failed to improve. In August 1946 the patient noted a number of tumor masses appearing in her skin.

Examination by us on Oct. 17, 1946 revealed a confluent erythematosquamous eruption with sharply demarcated borders, involving the scalp, face, forearms, the outer surfaces of the upper portions of the arms, and the upper part of the chest and back. A similar eruption was also present on the thighs and lower parts of the legs. There was mild atrophy, at times retiform in appearance, in the patches on the chest and shoulders, and to a lesser degree involving all areas. Associated with this atrophy was a moderate to mild degree of telangiectasia. All the areas showed mild scaling. Clinically, this eruption suggested that seen in subacute or chronic disseminated lupus erythematosus. However, associated with this eruption were multiple plaquelike tumors on the thighs, legs, face and neck. Some of the tumors were raised above the level of the skin approximately 1 cm. and varied in diameter from 1 to 4 cm. Several of the larger lesions showed an early tendency toward ulceration. A complete physical examination did not reveal enlargement of lymph nodes, liver or spleen, or other involvement of viscera. A clinical diagnosis of mycosis fungoides was made. The patient was admitted to the Buffalo General Hospital on November 1. A biopsy specimen removed from one of the tumors on the neck revealed pathologic change consistent with the diagnosis of mycosis fungoides. A biopsy specimen removed from an area of erythroderma on the back showed no specific pathologic change suggesting mycosis fungoides. The blood count done on November 2 was within normal limits. Roentgen examination of the chest showed a calcified node in the right hilar region and the pulmonary fields showed slight generalized fibrosis. On November 5 and for each of three successive days the patient was given 0.1 mg. of nitrogen mustard per kilogram of body weight. Each dose was given intravenously in 5 cc. of isotonic solution of sodium chloride. The patient tolerated the treatment well with the exception of nausea and vomiting following the first two injections. A moderate degree of anemia and leukopenia developed, which disappeared in four weeks.

Immediately after the completion of treatment, the skin showed considerable improvement with diminution in the amount of redness and scaling and a definite decrease in the size of all nodules. The itching had almost entirely disappeared. By the sixth day after treatment, the patient was subjectively much improved. Examination on December 5, approximately one

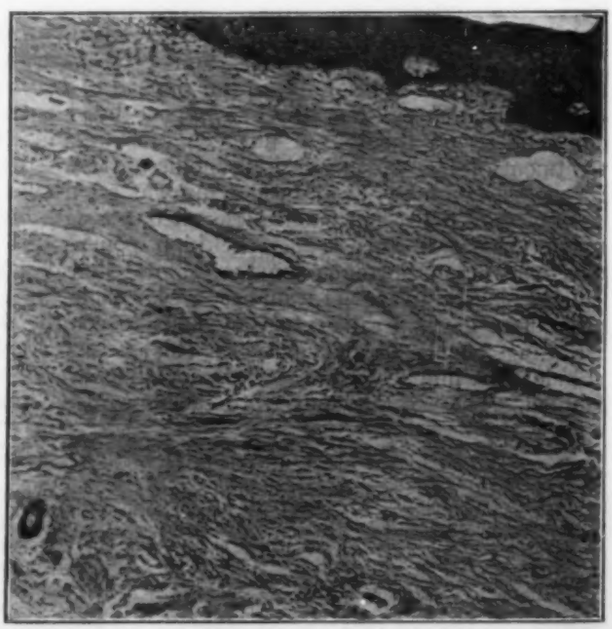

Fig. 2 (case 1).—Section of site of tumor taken one month after mustard therapy. Note absence of infiltrate. Hematoxylin and eosin; × 75.

month after her treatment, showed that most of the nodules had regressed completely and only a few could be slightly palpated. The diffuse erythroderma had improved at least 90 to 95 per cent, leaving some residual atrophy and telangiectasia. A biopsy taken from the site of a previous nodule on the right thigh revealed no evidence of mycosis fungoides microscopically. Examination on Jan. 23, 1947 revealed two active nodules,

one about 1 inch (2.5 cm.) in diameter on the right malar area and one about 3 inches (7.6 cm.) in diameter involving the right flank. The liver, spleen, lymph nodes and other viscera showed no evidence of involvement. The general surface of the skin previously involved with erythroderma showed no evidence of disease with the exception of mild atrophy and

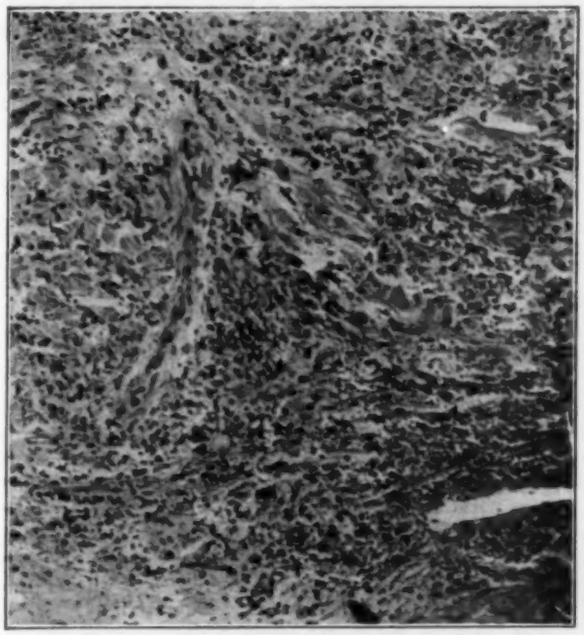

Fig. 3 (case 3).—Section of cutis from leg showing infiltrating cells of lymphosarcoma before nitrogen mustard therapy. Hematoxylin and eosin; × 75.

telangiectasia. Reports from her at her home, received on May 20, are that she has lost weight and that a large lump the size of an egg has appeared on her right arm. She complains of a mild itching.

CASE 2.—The diagnosis was mycosis fungoides. A. R. was a white man aged 62. Seven years previously an itching eruption developed on his back, and within a few weeks itching patches developed over the entire body with the exception of the hands, scalp and feet. These patches gradually became raised above the surface and itched intensely. After one and one-half years the patient noted the development of hard walnut-sized tumors in many of these patches. Examination by us in 1942 showed the typical clinical picture of mycosis fungoides, with many large plaques of all sizes covering the entire body with the exception of the face, scalp, hands and feet. There were fifteen to twenty tumor masses in these patches of all sizes from the smallest up to 10 cm. in diameter. A biopsy specimen removed from one of these tumors showed the typical pathologic change of mycosis fungoides. Adequate roentgen therapy with filtered and unfiltered radiation was recommended. The patient returned home and received careful radiation therapy for a period of approximately three years with great benefit. During the summer and fall of 1946, his condition became more exaggerated, with the formation of large infiltrated plaques and the development of numerous tumors, which no longer responded to radiation therapy. He was admitted to the Edward J. Meyer Memorial Hospital on Feb. 19, 1947. Examination showed a large number of plaque-like lesions of all sizes over the neck, shoulders, trunk and extremities. Between the raised infiltrated plaques there was a diffuse erythroderma with moderate scaling. In some of the large infiltrated plaques there were nodules of all sizes, the largest being about 6 cm. in diameter. A few of the larger nodules showed ulceration on the surface. In addition to the cutaneous findings, there were a number of hard walnut-sized deep inguinal nodes on both sides, associated with a moderate degree of edema of the scrotum and penis. The anterior and posterior axillary regions were particularly studded with nodules of all sizes, some undergoing early ulceration. Physical examination did not reveal enlargement of the liver or spleen or any other visceral pathologic change. Biopsy specimens removed from a nodule and from an area of erythroderma revealed the typical pathologic changes of mycosis fungoides. From a general point of view the patient was failing rapidly in weight, strength and appetite. The preliminary blood count showed a consistently low count of white blood cells, average approximately 4,000. The blood platelet count averaged approximately 170,000. However, in spite of the low white cell count a bone marrow puncture showed no reduction in activity. Roentgen examination of the chest showed exaggerated markings in the base of the right lung and spotty densities in the mediastinum.

On February 24 and for three consecutive days the patient received intravenously 0.1 mg. per kilogram of body weight of nitrogen mustard dissolved in 5 cc. of isotonic solution of sodium chloride. There was a severe gastrointestinal upset following the first two injections. After the last injection there was considerable accentuation of the erythroderma of the general skin surface other than the indurated plaques. There was also an increase in the ulceration of the tumors. However, by the end of the first week after treatment all the tumors had become soft and the plaques had lost most of their infiltration. The maximum improvement was noted on the eleventh day following treatment. Many of the plaques had completely disappeared, leaving residual hyperpigmentation. However, some of the plaques on the extremities improved only about 60 per cent and remained infiltrated. Twenty days after the completion of treatment, the inguinal nodes and edema of the scrotum and penis had completely disappeared but there was still infiltration in many of the plaques on the extremities. The intolerable itching had completely disappeared. Although the diffuse erythroderma had greatly improved it still persisted. It was decided to give this patient a second course of nitrogen mustard therapy of the same dosage. This was done on March 20 and on three successive days. There was little gastrointestinal reaction but immediately after completion of the treatment the patient manifested extreme weakness associated with palpitation and a persistent headache. The second course of treatment did not appear to improve materially the condition of the patient. Under adequate medical supervision and treatment, his blood count returned approximately to normal with the exception of the white blood cell count, which on the twentieth day following treatment showed only 2,850 cells. Roentgen examination of the chest showed no change. Biopsy specimens removed approximately two months after his first series of treatments showed essentially no change in the character of the infiltrate either in the residual nodules or in the erythrodermatous skin.

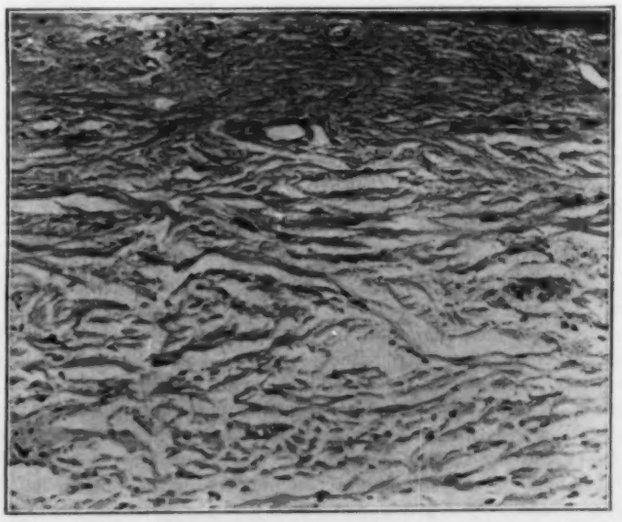

Fig. 4 (case 3).—Section of cutis from leg eleven days after nitrogen mustard therapy. The infiltrating cells have disappeared. Hematoxylin and eosin; × 75.

CASE 3.—The diagnosis was lymphosarcoma. A. P., a white man aged 61, was admitted to the Edward J. Meyer Memorial Hospital Oct. 15, 1946. He was comatose and jaundiced. Physical examination showed large firm nodes in the anterior cervical region bilaterally and similar nodes in both inguinofemoral regions. A mass was palpated in the right lower

Fig. 5 (case 5).—Appearance of patient before nitrogen mustard therapy.

quadrant of the abdomen and also an ill defined mass was felt in the left upper quadrant. There was edema of the right leg associated with multiple indurated bluish nodules involving the skin and subcutaneous tissue of the right leg below the knee. Some of the lesions were elevated about 2 cm. above the normal skin. Many smaller cutaneous and subcutaneous nodules were present in the area extending two thirds up the thigh. The liver and spleen were not enlarged. The white blood count was 4,650. Biopsy specimens taken from the skin and a lymph node revealed the presence of lymphosarcoma. In spite of the poor general physical condition of the patient and the feeling that he was moribund, it was decided to give him nitrogen mustard therapy. He was given the usual dose outlined in the previous 2 cases. Two days after the treatment the patient was mentally alert and the jaundice appeared to be subsiding. The lesions on the right leg became soft and continued to involute, until on the tenth day there was only residual pigmentation remaining in the skin. There was a decrease in the size of the abdominal masses and in the enlarged lymph nodes. His white blood cell count continued to fall in spite of multiple blood transfusions, and on the seventh day after treatment was 1,000 and on the tenth day was 850. Pneumonia developed and the patient died on the twelfth day after treatment. Autopsy performed on November 20 showed lobar pneumonia with fibrinous pleurisy and cardiac dilatation. There was no gross or microscopic evidence of lymphosarcoma in the lymph nodes, viscera or skin.

CASE 4.—The diagnosis was multiple hemorrhagic sarcoma of Kaposi associated with Hodgkin's disease. This case is included in this series because to date there have been no published reports on the effect of nitrogen mustards in Kaposi's disease. The patient, N. S., a white woman aged 67, was first seen in the dermatologic clinic of the Buffalo General Hospital in January 1946. At that time she had an eruption, chiefly on the arms, hands and legs, which consisted of purplish violaceous indurated nodules and tumors. The lesions were irregular in outline and varied in diameter from 0.5 cm. to 3 cm. A biopsy taken at that time revealed the typical pathologic changes of Kaposi's hemorrhagic sarcoma. Roentgen treatment was started. During June enlarged lymph nodes appeared in the axillas and neck. Biopsy of one of these nodes showed microscopic evidence of Hodgkin's disease. Because of this, she was admitted to the hospital on November 2, and the usual nitrogen mustard therapy was given. This treatment produced no change, either clinically or histologically, in the cutaneous lesions. There was likewise no effect from roentgen therapy.

CASE 5.—This case is included in our series although not one of lymphomatous nature because we wish to record the effects of nitrogen mustard on chronic disseminated lupus erythematosus. The patient, Mrs. G. S., white, aged 35, was first seen in 1943, at which time she had a weeping eruption about the eyes, face, neck and upper part of the chest. We first believed that she had contact dermatitis. She failed to respond to treatment for this condition, and during the next three year period the eruption continued to progress gradually to involve the arms and the upper part of the trunk. This was accompanied by extreme itching. Because of the severity of her cutaneous eruption, she was admitted to the Edward J. Meyer Memorial Hospital on Nov. 4, 1946. At that time she presented a bilateral and symmetric eruption most severe on the face, shoulders and upper parts of the arms. There were also lesions in the groin and two areas in the scalp. One area over the right frontal region about 2 inches (5.1 cm.) in diameter consisted of atrophic scarring and alopecia. There was a similar area over the postauricular region of the scalp. The lesions on the upper part of the trunk were sharply demarcated and somewhat infiltrated. It was the feeling of the dermatologists who examined her at that time that she was in the premycotic stage of mycosis fungoides. Lupus erythematosus was favored by one dermatologist. Biopsy specimens removed from the scalp and from the shoulder failed to be of any assistance in the diagnosis. Finally, because of the severity of the cutaneous involvement and the lack of response to all other therapy, including roentgen, it was decided to subject her to a series of treatments with nitrogen mustards, using approximately three fourths the usual dosage. There was mild nausea following the first and fourth injections. Two three days after completion of the treatment the patient had an unexplained rise in temperature to 102 F. rectally. On the fourth day after treatment, the eruption on the face, neck, arms and shoulders had faded at least 75 per cent and the itching had almost entirely disappeared. Her skin continued to improve steadily, and four weeks after treatment there was little to see on the face, neck, shoulders and arms except mild atrophy and some

Fig. 6 (case 5).—Appearance of patient six weeks after nitrogen mustard therapy.

telangiectasis. This was particularly noted over the face, ears and areas in the scalp. The patient's general condition improved remarkably. She gained weight and had an entirely different outlook on life. A biopsy specimen removed two weeks after treatment failed to reveal any distinctive pathologic change. However, three months after treatment a biopsy specimen removed from the right arm revealed the characteristic microscopic picture of lupus erythematosus. Since that time numerous other small patches of typical chronic discoid lupus erythematosus have appeared on both cheeks.

COMMENT

There is no question but that the 2 patients with advanced mycosis fungoides responded dramatically to the use of nitrogen mustard therapy. This effect, we believe, will in all probability be temporary. In case 1 we have a report that new nodules are appearing and in case 2 recurrences took place within four weeks after the treatment. In case 1 the eczematous manifestations of the disease, which were negative pathologically for mycosis fungoides, completely disappeared after nitrogen mustard therapy. In case 2 the diffuse erythroderma, which did show positive pathologic evidence of mycosis fungoides, although improving at least 90 per cent, still showed characteristic pathologic changes of the disease. It would seem to us that the value of nitrogen mustard therapy in the treatment of mycosis fungoides is limited principally to patients with far advanced disease, probably with internal lesions, who cannot be adequately treated with roentgen therapy or in whom the disease has become resistant to further radiation. It is obvious that further radiation therapy after the treatment with nitrogen mustard is essential. We are unable to state at this writing whether nitrogen mustard therapy will cause the lesions described in case 2 to be responsive to further radiation.

One immediate and dramatic effect of nitrogen mustard therapy in mycosis fungoides has been the early relief of the intolerable itching. This, of course, has a great psychologic effect on the patient.

The response of the cutaneous lesions in the case of lymphosarcoma was most dramatic. The pathologist was unable to find any gross or microscopic evidence of the disease, either in the skin or other tissues, twelve days after treatment.

In the 1 case of multiple hemorrhagic sarcoma of Kaposi, there was no response either clinically or microscopically to the use of nitrogen mustard therapy.

In some respects the effect of nitrogen mustard therapy in a case of chronic disseminated lupus erythematosus was the most startling and interesting which we have to report. This patient was treated with the idea that she probably had the premycotic stage of mycosis fungoides. It was subsequently proved that this was erroneous and that the diagnosis was really chronic disseminated lupus erythematosus. It is to be noted that three fourths the usual dosage of nitrogen mustard was given. We are not advocating the use of nitrogen mustard therapy in disease of a chronic inflammatory nature. The need for further study along this line is suggested. With the development of new drugs in the same series and safer dosage, these compounds may prove of value in treating some resistant inflammatory dermatoses.

ADDENDUM

Patient 1, with mycosis fungoides, relapsed, with fissural lesions, and is now bedridden. She is unable to return for further treatment. Patient 2, with mycosis fungoides, had a rapid recurrence and failed to respond to roentgen therapy. He died in September 1947. The patient with chronic disseminated lupus erythematosus (case 5) has continued to improve. Her skin is now free of all eruption except a few areas of chronic discoid lupus erythematosus on the face and neck. She has gained over 30 pounds (13.6 Kg.) in nine months.

ABSTRACT OF DISCUSSION

DR. CHARLES SPURR, Chicago: The application of the nitrogen mustard compounds to blastomatous dermatosis presents a new therapeutic tool to the dermatologist and warrants extensive investigation of the use of this drug in this group of diseases. As an adjunct to roentgen radiation it may offer a method of extending the period in which these patients will respond to therapy. This report and others demonstrate that the nitrogen mustards will produce a single remission. Of greater interest will be the effect of repeated courses of the drug in controlling the disease. At the University of Chicago Clinics we have seen favorable remissions in 75 per cent of a group of 16 cases of lymphomas which had become roentgen resistant. It is reasonable to expect similar results in this group of dermatoses. The unusual case of Kaposi's sarcoma with Hodgkin's disease is of interest because here there is a multicentric tumor shown in tissue culture by Bloom to be a sarcoma derived from mesenchymal cells. It is a relatively differentiated tumor of connective tissue, tissue which cytologically shows little reaction to nitrogen mustard. In our series, which now includes 110 cases observed for periods up to forty-five months, we have learned several things which I believe may be worth emphasizing for those who may consider using the nitrogen mustards: 1. The material apparently has no selective action on the tumor cells and is equally injurious to the hemopoietic tissue. The marrow has a tremendous capacity to regenerate, but a period of six weeks is necessary before a full regenerative picture develops. The interval between courses of nitrogen mustard should be six to eight weeks if anemia and persistent leukopenia are to be avoided. Clinically, the cases which require treatment more frequently than every two months have a brief prognosis. 2. We have been alert to evidence of a cumulative effect on the hemopoietic tissue. Thus far cases in our group have accumulated doses up to 350 mg. As yet we find no evidence of a hypoplastic reaction. 3. In considering the adaptability of the nitrogen mustards to therapy of any disease, attention should be given to the basic histogenesis of the disease as Dr. Osborne has done in mycosis fungoides. Cells as slightly differentiated as plasma cell myeloma show no response, while neuroblastomas show striking but brief remissions. The undifferentiated but slowly growing tumors as Hodgkin's disease and some lymphosarcomas show the best response.

DR. LEON GOLDMAN, Cincinnati: Our results through the Nitrogen Mustard Project at the Cincinnati General Hospital, under Dr. Eugene Sterne, have in general paralleled those of Osborne, at least in regard to mycosis fungoides, essentially an initial and temporary improvement. We had only 3 cases of mycosis fungoides. Postmortem studies were done in 1 of our patients at the Cincinnati General Hospital who contracted jaundice after nitrogen mustard therapy was started in the terminal phase. It was the opinion of the pathologist that this hepatic damage could have been due to the infection and toxemia which accompanied the terminal phase of the mycosis fungoides. From a casual survey of mycosis fungoides at present, it is disturbing, as Osborne and also Kierland indicate, that the biopsies reveal no decided changes at least at the end of therapy. Another of our patients, who had in addition to typical tumors an unusual verrucous reaction of mycosis fungoides on the lower extremities, revealed in the pretreatment biopsy of a lesion on the leg little specific infiltrate. However, in the post-treatment period the infiltrate was definite and typical. The pronounced acanthosis noted previously was sharply dimin-

ished. Newman (personal communication) has reported a cellulitis type of drug eruption from nitrogen mustard. It is probably through repeated cutaneous contacts, rather than by parenteral administrations, that eczematous hypersensitivity may develop. Karnofsky (personal communication) has indicated that a solution of nitrogen mustard was applied to local leukemic cutaneous infiltrations "but no beneficial result was obtained." Perhaps hydrolysis of nitrogen mustards is one of the chief difficulties of using these agents topically. We have used the older sulfur mustard agent in the treatment of papilloma. We have initiated a study of topical therapy with nitrogen mustards in condylomata acuminata where better penetration and absorption with the agent may be secured. Radioactive phosphorus, by the way, has also been used topically (value?). The initial experiment of Osborne and his group on the nucleotoxic activity of the nitrogen mustards in chronic inflammatory dermatoses is certainly stimulating, and it is hoped, although the temptations are so great, that only critical and careful work will be done. Current studies on nucleotoxic activity as related to viruses should concern the dermatologist also. I should say also that dermatologists should be more aware of the extensive developments in the field of enzyme chemistry.

DR. FRANK J. EICHENLAUB, Washington, D. C. I should like to report briefly on a patient aged 80 with reticulum cell sarcoma with tumors of the skin and with a mass in the chest which caused dysphasia. After failure of roentgen therapy, nitrogen mustard was administered. After the second course of nitrogen mustard leukopenia and anemia rapidly developed, and the patient died within a few days, in spite of the usual measures used to control this. The interesting feature about the case was that we have probably the earliest biopsies from both the skin and the mass in the mediastinum that I know of following the use of this drug and a death presumably from the drug. Sections show a complete disintegration of all the tumor cells. The other point is that the drug may be dangerous, and one should use it with great caution.

DR. RICHARD S. WEISS, St. Louis: I have had the opportunity of treating 1 patient with mycosis fungoides by means of nitrogen mustard. This was a Negro who had severe fungating lesions scattered over his body, with generalized erythroderma. He was treated in the way which Dr. Osborne described, and the erythroderma practically completely disappeared. The fungating tumors, when he was last observed about three weeks ago, had almost disappeared. His subjective condition was vastly improved and he expressed his determination to go back to work as a laborer. The striking response that Dr. Osborne mentioned of the erythrodermic features as well as the tumefaction was truly remarkable in this case. We shall try the drug on other patients when we get them and see whether we can duplicate these results.

DR. EARLE D. OSBORNE, Buffalo, N. Y.: I thank the discussers for their comments, especially Dr. Spurr for calling attention to the fact that the interval should be at least six to eight weeks between courses of nitrogen mustard. In large tumor clinics where many of these patients are being treated, we are inclined to be overenthusiastic, and repetition of the nitrogen mustard therapy within a period of three or four weeks is extremely dangerous. We feel certain about that, and anyone who has used this treatment must have suffered a few uncomfortable days or weeks. We need to know more about the cytology of tumors. Why do certain tumors respond and others not? Is it purely because of the maturity or place of derivation? Do we have inflammatory cells as a result of action on bone marrow, and so forth? Yet the inflammatory infiltrates disappear when there is no evidence pathologically in numbers of sections that there is any tumor cell or any monocytic derivative present, such as in our first case of mycosis fungoides. That is a curious thing, that the eczematous phase of mycosis fungoides without any pathologic change suggesting the disease clears up as readily as does the tumor and the erythroderma where the infiltrate is present. I have had no experience with topical applications containing nitrogen mustard.

DERMATOLOGY—THE INTERNATIONAL OUTLOOK

R. M. B. MacKENNA
London, England

Although most men and women spend their time in the turmoil of competition and the tumult of affairs it is noticeable that there are periods when large numbers of people pause to consider carefully the way ahead. Such a period occurred in Great Britain at the end of the last century, and after World War I many paused to consider the goals achieved and the matters which demanded attention. Now, after World War II (for these periods of retrospection and prospicience seem specially to occur either after cataclysmic events or at the junctions of recorded time), it would seem opportune to attempt to examine the dermatologic path which is ahead.

Such a survey can be divided into two sections; provided one uses the words in their widest connotations the first section may be called administrative and the second clinical.

DERMATOLOGIC ADMINISTRATION

Of administrative problems I select two for mention: the first is that in some countries there is danger lest dermatologists lose their independence in the corporate body of medicine, for many physicians seem eager to incorporate dermatology in their own purview. Further, in some countries industrial medicine is now recognized as a specialty and dermatologists will have to beware lest they are more and more excluded from this field which is so fruitful in dermatologic experience.

The second point concerns literature: textbooks and manuals will doubtless increase in number, and one can anticipate that they will soon be even more informative, more carefully produced and more lavishly illustrated than at present. It is the position in regard to journals which is disquieting. The average English-speaking dermatologist can keep abreast of recent work in his own field by a careful study of a relatively small number of publications; but these works deal chiefly in purely dermatologic matters. There is much work published in journals of anatomy, physiology, endocrinology, biochemistry, psychology and even statistics which has a bearing on his activities, concerning which he is often profoundly ignorant. The difficulty is enhanced by the fact that unless one has a special knowledge of these collateral branches of medicine one cannot accurately assess the value of the conclusions which have been reached by the authors concerned. It would seem, therefore, that there might be a useful scope for an international journal in which abstracts of papers likely to be of importance to the dermatologist were printed—each abstract to be followed by as careful an evaluation of the paper which has been abstracted as is possible at the time of publication. This evaluation should be in two parts: the first by a specialist in the subject under review, to explain intricate and technical points; the second by a dermatologist, to explain the application of the work to his own specialty.

The type of journal I visualize would be published not more often than three times a year. The editors would not be under any obligation to produce an issue

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of, say, sixty pages on each occasion; some numbers would be thick, others thin. The most careful discretion would be exercised in selecting papers. There would have to be a follow-up section; by this I mean that if a research project in physics was developing well from the dermatologic point of view and then failed to retain the interest of the physicists, the fact that no further publications had been made on this subject would be definitely stated at a convenient time in the journal.

The present would appear to be a useful period in which to launch such a periodical—for at last physiologists, biochemists and others are taking an interest in dermatology which they have never manifested before, and one of the factors which one can forsee in the way ahead is an increasing collaboration between members of this specialty and those interested in scientific and other branches of medicine. But despite this collaboration many of the collateral subjects are becoming increasingly technical and more difficult to follow. Liaison with colleagues in these branches must be perfected lest the dermatologist lose touch with advances of theirs which might be of benefit to him.

CLINICAL DERMATOLOGY

It is appropriate to commence this study of clinical dermatology by asking what lessons can be learned from the second World War? There are two principal answers to this question: first, the importance of the prevention of disease; second, the importance of the common dermatoses.

Lest any doubt that these are in fact the two major lessons of war it should be kept in mind that never before have armies been deployed in areas in which typhoid, typhus, malaria, dysentery, smallpox and all the great scourges of military forces are endemic with such freedom from these infections. The preventive work of the German Medical Corps was good, that of the Italians fairly good, that of the Japanese poor; but undoubtedly one of the reasons why the Allies won the war without leaving vast cemeteries to mark the sites of failures in preventive medicine was because of the hitherto unknown standards which were achieved in the armed forces. But unfortunately one has only to examine the morbidity from skin diseases in the Allied Armies or to study, for example, such figures as have been published concerning the United States army by D. M. Pillsbury [1] to appreciate the wastage in man-days, the economic loss and the amount of human suffering caused by the pyodermas and other common diseases of the skin, including scabietic infestation.

One of the matters which those who held posts of administrative responsibility were forced to appreciate during the recent war was that in the science or art of prevention, dermatology is at least forty years behind many other branches of medicine. Further, one has been forced to realize that because of the inherent difficulties of preventive dermatology most of the workers in this field have a convenient blind spot in their psychologic approach to their own subject, which insures that they do not trouble themselves greatly with regard to this problem except in certain limited fields such as industrial dermatoses, pyogenic diseases of the newborn and tinea.

1. Pillsbury, D. M.: Management of Bacteriai Infections of the Skin, J. A. M. A. **132**: 692 (Nov. 23) 1946.

Therefore I make no apology for submitting what the military would call "an appreciation of the situation" concerning this matter. The subject is one of international importance, for the prevention of disease is the ultimate goal of all medical endeavors. At the outset I would say that in this generation it is unlikely that dermatologists will progress very far in this matter; but although it will be for others to reach the goal, I should like my successors to look back and say that in this generation their course was set before them.

If one considers the lives of the persons living in cities and towns of Europe and North America, it can be stated with some assurance that besides the factor of relative economic prosperity there are four major factors which greatly influence the morbidity from skin diseases, for which dermatologists cannot claim any credit. These factors are: (1) the provision in dwelling houses or in convenient municipal premises of bathtubs, showers and hand basins with an adequate supply of pure water and a hot water system; (2) the provision of good quality, cheap soap for personal ablution; (3) facilities for washing and cleaning bedding and clothing, and (4) the standards of personal hygiene inculcated largely by tradition, custom and emulation. These standards are influenced by literacy, commercial advertisements and, to a degree which is not usually realized, by the effect of the cinema on population groups whose social customs lead them to emulate the better standards of living they see on the screen.

There are many other examples of active preventive measures in this field in which the dermatologist has had but little share, and yet which influence his work to a degree which—in the absence of statistics—one cannot now assess. But he cannot be content to continue to glean undeserved dividends from other men's work. How then can he begin actively to prevent disease in the community which he serves?

I suggest that one of the first things to be done is to assess the extent of the problems with which the dermatologist is confronted. The diseases which cause the majority of patients to apply for treatment are known from hospital records. But there is little or no accurate knowledge of the morbidity rates of skin diseases in the population groups concerned, for many persons who suffer from minor dermatoses, which cause much economic loss, never come to the hospital for treatment.

A certain amount of recently acquired data is available in many countries from the reports of school medical officers and from the records of service intake centers concerning the results of medical examinations of conscripts and recruits, but this information is obviously limited to selected groups of the population and is not valid for the whole.

I suggest that what is required is a series of surveys made by dermatologists among urban and rural communities in each country to determine the cutaneous maladies which are most prevalent in each social group; it would probably be advisable to correlate these observations with other data such as income limits, diet and occupation. By a suitable method of random sampling the numbers interviewed would not have to be vast, but they would be considerable.

I appreciate—of course—that such surveys are difficult to organize and carry through: sectional interests will always oppose schemes of this type, and the investi-

gators are likely to encounter latent and possibly active hostilities. But unless basic data are obtained in some such way one does not really know the extent and the most important factors of the problems with which the dermatologist is confronted.

I have little doubt that the results would be surprising. The old story that psoriasis is common amongst Greenland's icy mountains and rarely seen on India's coral strand would probably be finally disproved. I hazard a guess that pyodermas and maladies in which the seborrheic state is a fundamental factor would be found to be much commoner in civilian life than is at present recognized.

After one has considered the basic problem of assessing the morbidity rates for cutaneous diseases, one must turn briefly to the etiologic factors of a clinical nature which will have to be considered by any one interested in preventive dermatology. At the lowest estimate they are six in number: (1) genetic; (2) bacterial or fungous or virus; (3) biochemical; (4) psychologic; (5) allergic, and (6) nutritional. It is the conscious and subconscious realization of the significance of this list which makes so many shrug their shoulders whenever any one mentions preventive dermatology and turn to matters which appear to have more immediate importance.

It has to be faced that diseases of the skin which are genetic in origin are the least promising from the preventive aspect. Parentage may be denied with advantage to the community to those exhibiting maladies which are categorized as being dominant; denial of parentage to those believed to possess a disease of a recessive character would do little to reduce the incidence of the condition in the population.

Of the maladies which are bacterial or fungous in origin only the staphylo-streptodermas and certain problems in regard to tinea will be considered. The prevention of pyoderma and the infective dermatoses will depend, first, on impregnable proof of their bacterial causation (I have discussed this matter elsewhere and do not propose to consider it further here) and second, on an increase of the knowledge of biochemical processes; for example a good deal more must be known about the mechanism of autogenous disinfection of the skin, the X factor of Bigger and Hodgson [2] and the carbohydrate metabolism of the skin (Urbach and Lenz [3]). Not one of these is an insoluble problem, and if I am correct in suggesting that pyodermas are a fruitful source of sick-wastage in civilian as well as in military life, the sooner they are solved the better.

Superficial fungous diseases offer some interesting problems. In the British Isles I have read with much interest the recent papers in publications of the American Medical Association concerning this matter; it is appropriate to refer particularly to the paper by Schwartz and associates [4] concerning the control of ringworm of the scalp in school children in Hagerstown, Md., wherein reference is particularly made to barbers' implements as being an important source of spread of tinea capitis.

The control of superficial fungous diseases is in some ways a straightforward matter for hygienists. From the dermatologic point of view there are several matters of clinical interest. First, there is the influence of sex on many forms of the malady. Tinea capitis due to Microsporon audouini disappears at puberty. In my experience tinea of the glabrous skin is much less common in adult females than in men, but I wonder if this is a valid observation. Tinea cruris is much commoner in men than in women. Secondly, as far as England is concerned, tinea pedis is not a common malady. I suggest, with some temerity, that nowhere is it as common an endemic disease as is generally believed.

It is in the biochemical aspect of disease causation that many of the most interesting and important advances are going to be made during the next twenty years at least.

I have already emphasized my belief that many common maladies have a seborrheic background, and I am sure that if the problem of preventing the development of the seborrheic state can be solved much will have been done to relieve human suffering.

It has now been recognized by H. W. Barber [5] (1947) that the seborrheic triad of organisms as a primary cause of seborrheic diseases need no longer receive as much attention as formerly. He and Bishop have shown—I believe, conclusively—that in the causation of acne vulgaris the secretion and use of androgens is of paramount importance, and that the malady may be cured by the administration of estrogens. It is worthy of comment that the acne of an adolescent girl suffering from this disease may be extremely troublesome, although her menses are regular and her sexual organs and her secondary sexual characteristics are developing normally. Yet her acne may be cured or greatly improved solely by the administration of estrogenic hormones.

As far as is apparent there can be only one of four explanations: (1) the skin may be hypersensitive to androgens; (2) there may be a relative increase in the amount of androgens in the circulation; (3) there is a fraction of estrogenic hormone which exerts a specific effect on the skin, or (4) by analogy with the work of Urbach and Lenz [3] concerning skin diabetes one may postulate that just as the skin may vary from other tissues in its use of the hormone insulin so also it may vary from other tissues in its use of the hormone estrogen. In seborrheic maladies there may well be a linkage between the abnormal use of these two hormones. At the present time it would seem that the key to a proper understanding of these diseases is an increase in knowledge of the biochemistry of certain secretions of the endocrine glands. Until the dermatologist has found that key and learned how to use it, the prevention of seborrheic diseases is likely to be an insoluble problem.

In the prevention of many forms of psychosomatic skin diseases the education of general practitioners and of those of the laity who are educable is the most important step. Admittedly the dermatologist will have to increase, confirm and strengthen his own knowledge before he can teach others with assurance and safety. But the time is near when one will be able to say "Give me an accurate psychologic estimate of any patient and I will tell you the type of skin eruption which he is most likely to develop if—and, at present, it is a big 'if'—if he develops a cutaneous disease." One

2. Bigger, J. W., and Hodgson, G. A.: Lancet **1**: 544, 1943.
3. Urbach, E., and Lenz, J. W.: Carbohydrate Metabolism and Skin, Arch. Dermat. & Syph. **52**: 301 (Nov.-Dec.) 1945; correction, ibid. **53**: 277 (March) 1946.
4. Schwartz, L.; Peck, S. M.; Botvinick, I.; Leibovitz, A. L., and Frasier, E. S.: Control of Ringworm of the Scalp Among School Children, J. A. M. A. **132**: 58 (Sept. 14) 1946.
5. Barber, H. W.: Contribution to Modern Trends in Dermatology, London, Butterworth & Co., Ltd., 1946, to be published.

has to remember, of course, that the prevention of psychosomatic disease may be extremely dangerous and undesirable for the patient. Many patients must, from time to time, find some method of escape from their environment and from the pressure of their affairs. If a patient whose skin is an "organ of stress" is denied the use of that organ for purposes of "escape," and if there is no equally satisfactory means of elusion, he may easily become insane or commit suicide, or he may develop somatic symptoms of a much graver nature than, say, lichen planus or eczema.

Nevertheless, provided these dangers are fully appreciated, an enormous amount—probably much more than the specialist can achieve—can be done by general practitioners to insure that psychosomatic skin diseases are aborted or prevented.

The subject of prevention of allergic disorders follows easily on this brief reference to psychosomatic ills, for in many allergic states there is a psychopathic background and there may be two trigger factors: one psychologic and the other a specific allergen. I am not going to pause long in this survey to consider the prevention of allergic dermatoses—for two reasons. First, I believe that more is known about allergy in America than in England and second, the whole aim of the allergist's life is either to desensitize his patients or to teach them how to avoid exposure to the antigens or allergens to which they are sensitized—which is surely an excellent form of preventive dermatology.

There is but one aspect concerning nutrition to which I wish to refer, and that is the possible application of present clinical knowledge concerning calciferol (vitamin D_2) to the prevention of tuberculosis. At the present time this looks like the wildest shot in the dark, especially as Feeny, Sandiland and Franklin[6] have recently stated that the administration of this vitamin failed to improve pulmonary tuberculosis in a small number of cases. In this series the vitamin appears to have been cautiously administered, but it is interesting to note that 2 of the patients had lupus vulgaris as well as pulmonary tuberculosis, and although their lupus improved the condition of their lungs did not. Further, those who have used vitamin D_2 with care have been perturbed at the slow rise in blood urea which occurs in some instances, and which may indicate that the price paid for the cure of the lupus is some degree of permanent damage to the kidneys. But it is difficult to believe that this vitamin will only cure tuberculous lesions of the skin, especially as there is already some evidence of its beneficial effect when used in the treatment of surgical forms of tuberculosis. If the hazards of its use can be reduced, its therapeutic efficiency in all forms of tuberculosis enhanced and its mode of action fully ascertained then possibly medical science may have come near to one of its goals, the prevention of one of the greatest scourges of mankind.

So much for this brief appreciation concerning the position of preventive dermatology; I have made many omissions; for example, the position concerning preventive measures in occupational dermatoses has not been mentioned; yet those interested in this facet of dermatology have been pioneers. But I have said enough to focus the spotlight of attention on the subject of prevention and to indicate that in some matters the subject is not so hopelessly theoretic as many authorities believe.

Doubtless in the coming years there will be great advances in therapy; we shall try many things and "cleave to that which is good." As more is learned about them, the antibiotics may become more useful, and emulgent bases may prove worthy substitutes for the greases that have hitherto been used; the introduction of the use of radioactive isotopes to dermatologic practice may make enormous differences in technic; there will be more and more use of synthetic endocrine substances; therapy will in fact become more precise and less and less a matter of trial and error. Adequate facilities for the rehabilitation of persons who have had skin diseases will become widely available. Psychiatry and dermatology are at present in the stage of courtship. When they have been properly wedded the fruits of their union should be of inestimable benefit. The dermatologist will have to beware lest in learning so much that is new he forget some of the old knowledge that is so valuable.

Among other matters I have made a plea for a better liaison with the work relevant to dermatology which is being done in collateral branches of science and medicine; I have stressed my belief that the time has come when more than lip service should be given to the problems of preventive dermatologic practice and the common dermatoses.

In future years in Europe, the quick acuity and forceful logic of the French school, the clinical acumen of the Danish, Norwegian, Belgian and certain other schools will be felt. The British will, I hope, retain that flair for dermatology which they are said to possess, and I hope that occasionally they or their colleagues—will pluck another treasure as interesting as penicillin from the jealous hand of Aesculapius.

Scientific contributions may be expected from Portugal, Spain, Italy and the Levant. Judging by the wealth of clinical material that I have seen there, Iraq should also contribute her quota. India might solve the problem of prickly heat and contribute much to the knowledge of leprosy. The Schools of South Africa, Australia and New Zealand may steal some marches, but the British have their eyes on the whole American Continent. Here there is the resource and initiative, the ability and the zest, the material and the tradition. "The lot is fallen unto you in fair ground. Yea, you have a goodly heritage." Good luck in the exploitation of that heritage. Good hunting in the field of international endeavor.

Britain by its friendly competition intends to make America ride hard if it is to be the leader: but eventually, I hope, later generations, when they consider the very great work which this generation of dermatologists in the United States has accomplished, will adapt the famous words of Horace[7] to refer to the successes that have been achieved:

> Exegi monumentum aere perennius
> Regalique situ pyramidum altius, . . .

For (you) "have raised a monument (of endeavour) more enduring than one of brass, and loftier than the pyramids of kings; a monument which shall not be destroyed by the consuming rain, or by the mad rage of the North Wind or by the countless years and flight of ages."

6. Feeny, P. J.; Sandiland, E. L., and Franklin, L. M.: Lancet 1: 438, 1947.

7. Horace: Odes, Book 3, verse 30.

CHRONIC AURICULAR FIBRILLATION

Its Treatment with Quinidine Sulfate

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Since Frey [1] first recommended quinidine sulfate for the treatment of auricular fibrillation, much has been written concerning its merits and disadvantages in this disorder. Various workers [2] have expressed the opinion that auricular fibrillation is merely a manifestation of the unfavorable progress of otherwise severe heart disease and that in itself it does not materially alter the health of the patient or interfere with cardiac efficiency. Others,[3] however, have stated the belief that the development of auricular fibrillation adds to the cardiac insufficiency and carries with it certain dangers. The problem is unsettled and warrants further clinical and laboratory investigation.

THE EFFECTS OF AURICULAR FIBRILLATION

The experimental production of auricular fibrillation in animals reduces the output of the heart by an average of 40 per cent.[4] It is doubtful that auricular fibrillation causes such a pronounced reduction of function in the already failing heart, but it is certain that any reduction in cardiac efficiency occurring with the advent of this arrhythmia is of grave significance. Furthermore, studies [5] of gases in the blood, made before and after the restoration of normal rhythm in patients with auricular fibrillation, have shown that the efficiency of the cardiorespiratory mechanism is greater under normal rhythm than during fibrillation, although the ventricular rate was slower before the rhythm was restored to normal.

Occasionally one sees patients in whom the appearance of auricular fibrillation is followed shortly by the first signs and symptoms of congestive failure. In such instances it would appear that the advent of auricular fibrillation is the important factor in precipitating congestive failure. In spite of opinions to the contrary,[2b, c] we believe that the presence of auricular fibrillation does materially alter the well-being of the patient and exposes him to certain hazards, which are far less imminent after reversion to normal sinus rhythm. The danger of intra-auricular formation of thrombus with subsequent embolic phenomena is present as long as the auricles continue to fibrillate. It is believed that congestive failure is likely to be perpetuated by auricular fibrillation.[3b] Lastly, the subjective symptoms of palpitation engendered by the cardiac irregularity, even in digitalized patients, are frequently distressing and often lead to more or less severe cardiac neuroses.

DANGERS OF QUINIDINE THERAPY

So much has been written about the toxicity of quinidine [6] and the danger of toxic reactions that this valuable drug has been withheld in many cases when its use might have improved the patient's cardiac status.

The possibility of embolism occasioned by the use of quinidine should not be considered. Laws and Levine have shown that 11.5 per cent of deaths from rheumatic heart disease occur as the result of emboli and thrombi.[7] In their study all except 1 of 17 patients with embolic or thrombotic processes had auricular fibrillation. Viko, Marvin and White [8] stated that it seems justifiable to conclude that embolism occurs less frequently under quinidine therapy than under ordinary therapy. In 200 cases of auricular fibrillation without quinidine therapy, these investigators observed 9 instances of embolic phenomena (4.5 per cent), whereas in 484 cases of auricular fibrillation treated with quinidine emboli occurred in only 15 cases (3.1 per cent).

The toxic reactions of quinidine commonly described in the literature are numerous and have been well summarized by Carter.[6c] Toxic manifestations occurred in 64 per cent of the patients in our series. In 54 per cent the symptoms were mild, including nausea, anorexia, vomiting, headache, drowsiness and tinnitus. Severe reactions, including syncope, peripheral vascular collapse, pulmonary embolism and delirium, occurred in 10 per cent. Temporary asystole occurred in 1 case, thirty-six hours after normal rhythm had been established and the dose of quinidine reduced; fibrillation returned twenty hours after the drug was omitted.

The contraindications to quinidine therapy listed in the literature embrace practically all those conditions commonly found in patients with auricular fibrillation. The contraindications most frequently mentioned are: senility, bacterial endocarditis, extensive valvular disease, auricular fibrillation of long duration, coronary occlusion, heart failure, hyperthyroidism, angina pectoris relieved by fibrillation, complete auriculoventricular block, history of emboli and history of sensitivity to quinidine. We do not agree that the majority of these conditions constitute real contraindications to the use of the drug. Except for bacterial endocarditis, complete block and angina relieved by fibrillation, every one of these problems has been present in some patient in our series; yet treatment with quinidine produced few serious complications.

SELECTION OF CASES

There is some agreement that quinidine has a certain field of usefulness in the treatment of auricular fibrillation, although it is also agreed that not all patients with this arrhythmia should receive quinidine.[9] Askey [3a] stated: "One must ask in every case of auricular fibrillation with congestive failure whether quinidine should be given a trial. It is impossible correctly to predict in the individual case whether the patient will be benefited

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1. Frey, W.: Ueber Vorhofflimern beim Menschen und seine Beseitigung durch Chinidin, Berl. klin. Wchnschr. **55**: 450, 1918.

2. (*a*) DeGraff, A. C., and Lingg, C.: The Course of Rheumatic Heart Disease in Adults; The Influence of Auricular Fibrillation on the Course of Rheumatic Heart Disease, Am. Heart J. **10**: 630-642 (June) 1935. (*b*) Kohn, C. M., and Levine, S. A.: An Evaluation of the Use of Quinidine Sulfate in Persistent Auricular Fibrillation, Ann. Int. Med. **8**: 923-938 (Feb.) 1935. (*c*) Stroud, W. D.; La Place, L. B., and Reisinger, J. A.: The Etiology, Prognosis, and Treatment of Auricular Fibrillation, Am. J. M. Sc. **183**: 48-60 (Jan.) 1932.

3. (*a*) Askey, J. M.: Quinidine in the Treatment of Auricular Fibrillation in Association with Congestive Failure, Ann. Int. Med. **24**: 371-384 (March) 1946. (*b*) Korns, H. M.: An Experimental and Clinical Study of Quinidine Sulfate, Arch. Int. Med. **31**: 36-55 (Jan.) 1923. (*c*) Fahr, G.: Treatment of Cardiac Irregularities, J. A. M. A. **111**: 2268-2275 (Dec. 17) 1938.

4. Eyster, J. A. E., and Swarthout, E. C.: Experimental Determination on the Influence of Abnormal Rhythms on the Mechanical Efficiency of the Heart, Arch. Int. Med. **25**: 317-324 (March) 1920.

5. Stewart, H. J., and Carter, E. P.: Blood Gases in Auricular Fibrillation and After Restoration of the Normal Mechanism, J. A. M. A. **78**: 1751 (June 3) 1922.

6. (*a*) Wolferth, C. C.: Depression of Cardiac Conductivity During Quinidine Therapy, J. A. M. A. **80**: 1289-1291 (May 5) 1923. (*b*) Berman, R., and Blumenthal, J. S.: Quinidine in Auricular Fibrillation, Minnesota Med. **25**: 198-200 (March) 1942. (*c*) Carter, J. B.: Uses and Abuses of Quinidine, M. Clin. North America **29**: 215-228 (Jan.) 1945.

7. Laws, C. L., and Levine, S. A.: Clinical Notes on Rheumatic Heart Disease with Special Reference to the Cause of Death, Am. J. M. Sc. **186**: 833-849 (Dec.) 1933.

8. Viko, L. E.; Marvin, H. M., and White, P. D.: Clinical Report on the Use of Quinidine Sulfate, Arch. Int. Med. **31**: 345-363 (March) 1923.

9. Askey,[3a] Berman and Blumenthal,[6b] Carter.[6c]

or harmed—only trial can determine this." Since quinidine is generally considered a dangerous drug, definite criteria are needed for the selection of patients for treatment. A better understanding of the untoward reactions likely to be produced by the drug is also desirable.

Electrocardiographic records and direct visualization of the auricles at operation frequently show apparently adequate auricular contractions interrupting the fibrillation. We believe that the occurrence of such effective contractions in fibrillating auricles would tend to loosen mural thrombi as readily as would normal auricular activity.

In patients with congestive failure persisting after complete digitalization, rest, diuretics and a low sodium diet, the administration of quinidine to abolish auricular fibrillation sometimes produces remarkable improvement. By relieving palpitation and improving the patient's sense of general well-being quinidine may do much to prevent the development of a cardiac neurosis. If normal rhythm can be restored, patients who have despaired because they have been told that their outlook was hopeless often leave the hospital greatly improved—in spite of the fact that there has been little increase in the measurable efficiency of their hearts.

MATERIAL

Fifty unselected cases of auricular fibrillation were studied. Two patients in this group had had fibrillation for only a few days, at most. There may be some question as to whether they should be included in a study of chronic auricular fibrillation. In both cases, however, the patients were pursuing a rapid downhill course until auricular fibrillation was controlled by quinidine. All other patients had well established auricular fibrillation which had been present for periods ranging from two weeks to many years. Of the 50 patients, in 44 (88 per cent) normal rhythm was restored, and normal rhythm persisted up to the time of writing (one month to two years) in 25 (50 per cent).

In table 1 the cases are classified according to the types of cardiac lesions present. Forty-six per cent of the patients had rheumatic heart disease; 32 per cent had arteriosclerotic heart disease, and the remaining 22 per cent had thyrotoxic heart disease, hypertensive cardiovascular disease or combinations of these conditions.

Table 1 also classifies the patients according to age, duration of fibrillation and degree of cardiac failure. The latter was judged according to the New York Heart Association Functional Classification.

METHOD OF STUDY

All patients were admitted to the hospital and observed for several days before quinidine treatment was begun. Repeated electrocardiograms were made before, during and after quinidine therapy. Complete digitalization was effected in each case before quinidine therapy was instituted. An attempt was made to observe changes in cardiac efficiency, before and after reversion, by daily measurements of vital capacity and by determinations of the venous pressure and circulation time. No difficulty was experienced by giving digitalized patients enough calcium gluconate to determine the circulation time according to the arm to tongue method. A 2 meter roentgenogram of the chest and a fluoroscopic examination of the barium-filled esophagus were made before and after reversion to normal sinus rhythm in a large percentage of the patients. The roentgen studies failed to show consistent changes in the size of the auricles. Indeed, in some cases the size of the auricles increased even when the patient was greatly improved subjectively. Careful determinations of the vital capacity were made in 18 patients of this series, and an average increase in vital capacity of 270 cc. was observed with return to normal rhythm. In the 13 patients whose venous pressure was estimated before and after reversion, an average decrease in venous pressure of 20 mm. of saline solution was found. In 14 patients the circulation time decreased an average of 6.7 seconds.

DOSE OF QUINIDINE

All of the patients in this series were given quinidine sulfate according to a fixed plan, whenever this was feasible. A test dose of 0.2 Gm. was given first. If no toxic manifestations were seen within twelve hours, the drug was then given every four hours, day and night. The dosage was begun at 0.2 Gm., and increased by 0.2 Gm. every twelve hours until normal sinus rhythm occurred, until toxic symptoms appeared or until the dose of 0.8 Gm. was reached. In patients requiring more than this amount, further increases in dosage were made more slowly—usually 0.1 Gm. per dose every twenty-four hours. Our studies have convinced us that the drug has some cumulative effect. In several patients who had minor toxic reactions which precluded further increase in dosage, reversion to normal rhythm occurred after two to three days on the same dose. In 4 patients the rhythm reverted to normal three to eight hours after cessation of therapy. The mechanism of these reversions is not completely clear, but it seems likely that an accumulation of quinidine may explain them. In some cases of auricular fibrillation quinidine may produce fixed auricular flutter.

TABLE 1.—*Percentage Distribution of Patients According to Type of Basic Cardiac Lesion, Age, Duration of Fibrillation and Degree of Cardiac Failure*

Type of Heart Disease	Incidence, Percentage	Age	Incidence, Percentage
Rheumatic	46*	10-19	4
Arteriosclerotic	32***	20-29	8
Thyrotoxic	4*	30-39	16*
Hypertensive	2	40-49	20*
Mixed	16*	50-59	16*
		60-69	18**
		70-79	14
		80-90	4*

Duration of Fibrillation	Incidence, Percentage	Degree of Cardiac Failure	Incidence, Percentage
Unknown	22**	0	4
1 month	6	I	16**
3 months	12*	II	30**
6 months	24*	III	16*
12 months	6	IV	34*
2 years	8*		
4 years	4*		
4-22 years	18		

* Each asterisk represents one failure to revert to normal rhythm.

MAINTENANCE DOSAGE

Since the omission of quinidine after reversion to normal rhythm is followed in many cases by a prompt return of the auricular fibrillation, we placed most of our patients on maintenance doses of the drug. No known method is available for estimating in advance the necessary maintenance dosage. Some patients after

reversion maintain normal rhythm for long periods of time without quinidine. Harris [10] reported that 57.7 per cent of his patients still had regular rhythm after six months, and 36 per cent after one year. In other reports the incidence of patients who maintained normal rhythm for six months without quinidine varies from

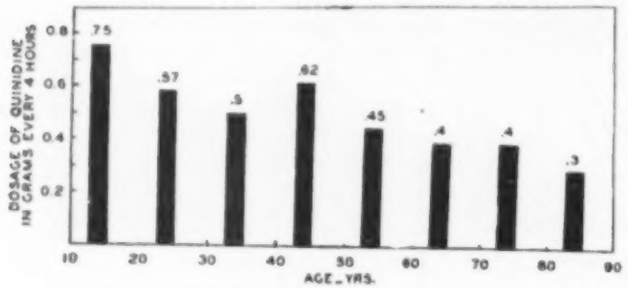

Chart 1.—Dosage of quinidine in grams per four hours required to restore auricular fibrillation to normal rhythm in various age groups.

28.2 per cent [11] to 42.8 per cent.[12] Since the patients in these groups were selected and had less seriously damaged hearts than those in our series, there was probably less tendency for them to return to fibrillation.

The dosage of quinidine was usually reduced within twenty-four hours after the rhythm returned to normal. In most cases the same dose was given at six hour intervals instead of four hour intervals. If normal rhythm persisted, the dose was further lowered in some cases. The average maintenance dose, given every six hours, was 0.17 Gm. less than the four-hourly dose necessary for reversion. In 35 patients for whom a satisfactory maintenance dosage was worked out, the average amount necessary for reversion was 0.45 Gm. every four hours, and the average maintenance dose 0.28 Gm. every six hours.

Charts 1 and 2 illustrate the average four hourly dose of quinidine necessary to cause auricular fibrillation to revert to normal rhythm in the different age groups and etiologic groups. The important factor in

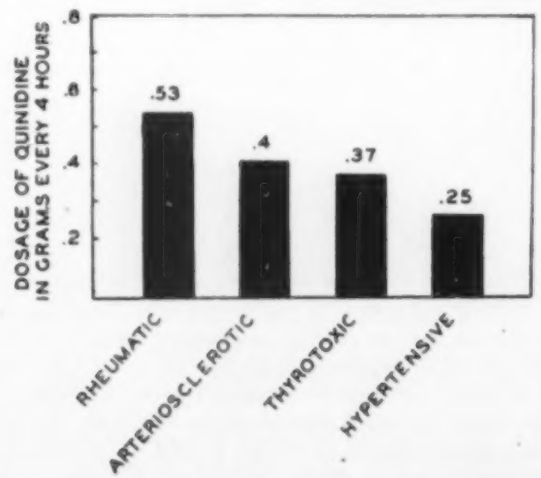

Chart 2.—Dosage of quinidine in grams per four hours required to restore auricular fibrillation to normal rhythm in various causal types of cardiac disease.

10. Harris, K. E.: A Series of Cases of Auricular Fibrillation Treated with Quinidine Sulfate, with Special Reference to the Duration of the Restored Normal Mechanism, Heart **14**: 283-288 (March 24) 1929.
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dosage is probably the etiology of the heart disease underlying the auricular fibrillation; the smaller dosage necessary in the older age groups is believed to be a reflection of this factor.

RESULTS

Table 2 presents an analysis of the 44 cases in which normal sinus rhythm was restored, showing the duration of normal rhythm and whether or not it was eventually terminated by return to auricular fibrillation or by death. The center column indicates the number of patients still having regular rhythms at varying intervals of time.

It is apparent that failure to revert to normal rhythm in this series bears little relationship to the degree of failure present, the age of the patient or the duration of fibrillation. Fairly definite significance can be attributed to the etiology of the underlying cardiac condition,

TABLE 2.—*Number of Patients Reverted to Normal Rhythm with Quinidine Who Later Had Return of Fibrillation, Normal Rhythm, or Who Died at Periods of One Month to Two Years*

Period of Observation	Return of Fibrillation	Still Regular at	Death
0-1 mo.	8	4	3
1-2 mo.	2	1	3
2-4 mo.	1	6	1
4-6 mo.	0	5	0
6-12 mo.	0	5	1
1-2 yr.	0	4	0

TABLE 3.—*Analysis of the Fourteen Patients Who Have Maintained Regular Rhythm for Periods of Four Months to Two Years*

Age	Etiology	Degree of Failure Before Therapy	Duration of Fibrillation	Individual Dose Necessary for Reversion
10-19.....2	Rheumatic.....9	0..3	1-4 wk.....2	0.2-0.3 Gm....7
20-29.....1	Arteriosclerotic..2	I..2	1-2 mo.....2	0.4-0.5 Gm....2
30-39.....2	Thyrotoxic.....1	II..5	2-4 mo.....3	0.6-0.8 Gm....2
40-49.....5	Hypertensive....1	III..2	2-10 yr.....3	0.9-1.1 Gm....2
50-59.....3	Rheumatic and	IV..2	Unknown..4	1.2 Gm.....1
70-79.....1	thyrotoxic.....1			

however. In every case of thyrotoxic heart disease treatment of the auricular fibrillation was unsuccessful prior to correction of the underlying hyperthyroidism. Five patients (10 per cent) of this series had thyrotoxicosis, either alone or in combination with advanced rheumatic heart disease. Two failures occurred (40 per cent). In one of these patients severe nausea and vomiting precluded the administration of sufficient quinidine; the other patient refused treatment. Three failures occurred in 16 patients with arteriosclerotic heart disease (a failure rate of 18.7 per cent), whereas in 23 patients with rheumatic heart disease treatment was unsuccessful in only 1 case—a failure rate of 4.3 per cent. The cases represented in the other groups are too few to permit statistical analysis.

Of interest are the 14 patients who have maintained a normal sinus rhythm for periods varying from four months to two years (table 3). Only 50 per cent of these patients are on maintenance doses of quinidine; consequently it is possible that in some of this group fibrillation again will develop and will require further quinidine.

Aside from the 2 patients in the age group of 10 to 19 years, both of whom appear in table 3, the patients in the 40 to 49 year age group stand out as having the

most favorable course; 50 per cent of the 20 patients in this group have had regular rhythm for four months or more. The doses necessary for the original reversion to normal sinus rhythm are shown in chart 1. It is apparent that patients whose auricular fibrillation was abolished on doses of 0.2 to 0.3 Gm. every four hours are most likely to maintain normal rhythm. It is also apparent, however, that the necessity for huge doses does not preclude a favorable course.

The etiology of the heart disease seems to be the dominant factor in the success of treatment (chart 2). Seventy-one and four-tenths per cent of the patients who still maintain a regular rhythm after four or more months had rheumatic heart disease.

DEATHS

Eleven of the 50 patients studied have died at the time of this report. Four of these patients had had no quinidine for more than four days at the time of their death. Four of the remaining 7 patients died outside the hospital, and no details were learned, aside from the fact that 1 patient died suddenly. This patient had rheumatic heart disease with mitral stenosis and aortic regurgitation. Autopsies were done on 2 of the 3 patients who died in the hospital and on 1 who died outside the hospital. Brief summaries follow:

1. This patient, a white man aged 40, was critically ill on admission and died on the sixth hospital day, four hours after the last dose of quinidine (0.4 Gm.). Death apparently was due to pulmonary edema. This patient's auricular fibrillation had not reverted to normal sinus rhythm. The autopsy showed evidence of cardiac failure, rheumatic pericarditis, mitral stenosis, rheumatic pleuritis, hydrothorax and ascites.

2. The patient was a white man, aged 72, whose cardiac rhythm had been normal for one month. He was on a maintenance dose of 0.2 Gm. of quinidine four times daily. He died suddenly while sitting in his automobile.

The observations at autopsy were as follows. Adhesive pericarditis, cardiac enlargement, dilatation of the left auricle, left ventricular hypertrophy, rheumatic mitral valvulitis, severe fibrinous pleurisy (left lung) and mild generalized atherosclerosis.

3. This patient, a white man aged 61, was critically ill on admission. Auricular fibrillation was restored to normal sinus rhythm by 0.6 Gm. of quinidine every four hours. Death occurred two days later, while he was on a maintenance dose of 0.4 Gm. four times a day.

The autopsy showed cardiac hypertrophy and dilatation; right auricular thrombus; mitral valvulitis, healed; bilateral pleural effusion; multiple small pulmonary infarctions, old and new; ascites; thrombosis of superior mesenteric artery, and generalized mild arteriosclerosis.

COMMENT

It is apparent that no definite rules can be set down for the use of quinidine in patients with auricular fibrillation. Best results are obtained in patients with rheumatic heart disease, who are easily restored to normal rhythm on small doses of the drug. In our series the patients in the age groups 10 to 19 and 40 to 49 showed the best responses.

In our opinion the only definite contraindications to the use of quinidine are severe conduction defects, subacute bacterial endocarditis and angina pectoris which has been previously relieved by the onset of auricular fibrillation. We believe that all other patients with chronic auricular fibrillation should be given a trial on quinidine, since there is no way of foretelling which ones will revert to normal rhythm on small doses of the drug. The likelihood of emboli is greater in those patients with auricular fibrillation than in those restored to normal rhythm. Treatment should be begun in the hospital, where electrocardiographic studies and close observation are possible.

SUMMARY AND CONCLUSIONS

Of 50 unselected patients with chronic auricular fibrillation treated with quinidine sulfate, 44 (88 per cent) were restored to normal rhythm. At the time this is written the rhythm remains regular in 20 of these patients (56.8 per cent), four weeks to two years after quinidine was started.

Quinidine sulfate is the most useful drug available for the restoration of normal rhythm in patients with auricular fibrillation. The use of quinidine is attended by certain dangers, but in general the incidence of serious cardiovascular accidents in patients treated judiciously with the drug is little, if any, greater than in similar patients treated without quinidine.

The return to normal rhythm is accompanied, in a large percentage of patients, by definite subjective improvement. Objective signs of increased cardiac efficiency are often seen, but improvement in various tests of function, such as vital capacity, has not been consistent.

Patients with rheumatic heart disease and patients with any type of heart disease whose auricular fibrillation reverts to normal rhythm on small doses of quinidine show a more noticeable tendency to maintain normal rhythm than do others. However, good results have also been obtained in other types of patients. There is no method of ascertaining what response is to be expected in a given patient.

Omission of the drug, either temporarily or permanently, at the onset of moderately severe symptoms or signs of toxicity will reduce the incidence of serious reactions.

In most patients maintenance doses of quinidine are necessary to prevent recurrence of the auricular fibrillation.

This study indicates that much larger doses of quinidine sulfate may be safely administered than has been thought practical by many observers.

More experiences in the use of quinidine in chronic auricular fibrillation should be recorded to define more clearly the usefulness of this drug.

ABSTRACT OF DISCUSSION

DR. GEORGE T. HARRELL, Winston-Salem, N. C.: Quinidine has been accepted for many years as a useful drug in the treatment of acute alterations of cardiac rhythm. Its use in chronic auricular fibrillation with cardiac failure should be emphasized. Eighty per cent of Dr. McMillan's group of patients were in congestive failure when administration of the drug was started; all were digitalized, and other measures of therapy had failed. The usually accepted contraindications for the use of quinidine therapy were ignored and the dangers were balanced against the benefits to be expected. The increase in cardiac efficiency and reduction in the degree of failure after the restoration of normal rhythm fully justified the risks. Emboli will occur in the course of auricular fibrillation, whether or not patients are treated with quinidine, because of the occasional strong auricular contractions which occur spontaneously. The dosage used was much higher than that usually thought to be safe. The maximum dose was 1.2 Gm. every four hours day and night with a total of 6 Gm. in twenty-four hours. Since the greater part of the quinidine is excreted in three to four hours, the night dose is especially important. The need for a maintenance dose over a long period of time, even in patients kept digitalized, is another point which has not usually been recognized. Whether the age of the patient or the

causation of the heart disease is more important in anticipating a beneficial effect is questionable. One would suspect that more cardiac damage would have occurred in the older than in the younger age group and that this would account for the smaller dosage necessary in it. It is probably wise to hospitalize the patient so that the occasional syncopal attack or minor toxic reaction—nausea or tinnitus—can be more readily controlled. Until we know more about its use in chronic auricular fibrillation, serial electrocardiograms should be taken at fairly frequent intervals and the drug discontinued at the slightest indication of any defect in auriculoventricular conduction. The subjective improvement observed as a result of the reduction in the severity of symptoms brings out the possibility of the prevention of cardiac neuroses. Quinidine gives the family physician a useful method of attack in previously hopeless cases.

THE RELATIONSHIP OF CHRONIC ALCOHOLISM TO ATHEROSCLEROSIS

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The diet of the average person is so varied, fluctuant and unmeasurable that it is not ordinarily possible to determine whether its composition is concerned in the pathogenesis of atherosclerosis. That dietary factors may play a role in this disease is suggested by the following observations: 1. Lipid, notably cholesterol, is a conspicuous constituent of the arterial lesions. 2. Feeding of cholesterol to rabbits is followed by the development of comparable arterial lesions. 3. Severe atherosclerosis is more likely to develop in obese than in underweight persons.[1] 4. Periods of wasting and loss of weight are usually associated with depletion of the lipid deposits in human arterial lesions.[2]

Dietary peculiarities of populations in different countries, such as have been compiled by Rosenthal,[3] cannot be readily related to the incidence of atherosclerosis. Other environmental factors, differences in racial background and in climatic and economic conditions may be involved. Moreover, since there is no standard measure of the atherosclerotic process, the findings of independent observers are not closely comparable.

In chronic alcoholism, however, certain generalizations about the composition of the diet are permissible. Those who consume a quart (0.95 liter) of whisky daily or its alcoholic equivalent derive considerably more than their entire basic caloric requirement from this alone, assuming that all its alcoholic content is absorbed and metabolized. It has been calculated that about 1,750 calories are provided by a pint (0.47 liter) of whisky.[4] Therefore consumers of even this lesser amount probably satisfy a large portion of their caloric needs with alcohol. It is obvious that such persons must as a rule consume relatively small amounts of other foods. One may conclude, therefore, that persons with chronic alcoholism as a group are maintained on low fat and protein diets.

If the development of atherosclerosis depends on the consumption of large quantities of fat, persons with chronic alcoholism should be singularly free from this disease. In 1904, Cabot[5] reported that atherosclerosis was uncommon in persons with chronic alcoholism under 50 years of age. His purpose, however, was to disprove the older belief that alcoholism promoted the development of arteriosclerosis. Since then many well qualified observers, including Wells,[6] Aschoff[7] and Leary[8] have expressed the opinion that chronic alcoholism is protective against atherosclerosis. This opinion appears to be based on impressions rather than on the detailed study of series of cases. A low incidence of atherosclerosis may be attributed, at least in part, to the fact that excessive users of alcohol die, on the average, at an earlier age than do moderate consumers or total abstainers.[9] Martland,[10] who has had wide experience with necropsy findings in chronic alcoholism, made the following pertinent comment: "In the great majority of cases, overfeeding and obesity rather than chronic alcoholism are the main causative factors in the rising arterial pressure of middle life and in the production of arteriosclerosis." He did not, however, suggest that chronic alcoholism might prevent the development of atherosclerosis. Weiss and Minot[11] and Wright[12] considered it unproved that chronic alcoholism retards the development of atherosclerosis. The only experimental evidence is that of Eberhard,[13] who found that feeding of alcohol together with cholesterol impeded the development of arterial lesions in rabbits. It has been suggested[11] that the solvent action of alcohol on lipids might be the mechanism by which the formation of atheromatous deposits could be inhibited. But even in severe alcoholic intoxication the concentration of alcohol in the blood seldom exceeds 0.50 per cent.[14] It is not likely that appreciable amounts of lipid are kept in solution at this low concentration.

During the past twelve years, 519 persons with chronic excessive alcoholism, 35 years of age or older, have been studied at necropsy at Bellevue Hospital, New York. The purpose of this communication is to report the incidence of atherosclerosis in this group as compared with that in a control group of 600 consecutive necropsies of total abstainers and moderate consumers of alcohol 35 years of age or older at death. The control group is designated for convenience hereafter in the text and tables as the "nonalcoholic" group.

METHODS

In approximately one half of the 519 alcoholic addicts the daily consumption of alcohol is known to have exceeded 1 pint of whisky or its equivalent in other forms of alcoholic beverages for many years. Persons are not included in whom lesser amounts of daily alcohol consumption were specified. In the remaining cases in the group of 519 the amount of alcohol consumed was not recorded, but the patients were stated to have consumed excessive quantities for long periods of time. Persons are excluded in whom the history of alcoholism

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was qualified by such terms as "moderate," "habitual" or "periodic" consumption or in whom alcoholism was not stated to have continued over many years.

The methods of grading the atherosclerotic process, the criteria for obesity and undernutrition, hypertension and cardiac hypertrophy have been described in detail in a previous analysis concerned with incidence of atherosclerosis.[1]

RESULTS

In the alcoholic group as a whole, atherosclerosis is considerably less common and less severe than in the control group of persons without or with moderate alcoholism (table 1). Furthermore, lesions that may be attributed to atherosclerosis of the coronary and cerebral arteries are only one half to one third as common in the alcoholic addicts as in the control series. It is also clear, however, that in excessive alcoholism both severe and moderate degrees of atherosclerosis may develop with some frequency.

The data in table 2 indicate that, as might have been anticipated, those who were excessively alcoholic died at a relatively young age. Three fourths of both men and women of the control series were 55 years of age or older at death. Only one half of the alcoholic men and one fourth of the alcoholic women survived beyond the age of 55 years. This difference may account partly or entirely for the low incidence of atherosclerosis and associated lesions in the alcoholic series.

TABLE 1.—*Incidence of Atherosclerosis and Associated Lesions in Persons with Chronic Alcoholism and in the Nonalcoholic Group*

Lesion	Alcoholic Group		Nonalcoholic Group *	
	Number	Per Cent	Number	Per Cent
Generalized atherosclerosis				
Marked	67	12.9	147	24.5
Moderate	165	31.8	238	39.7
None or slight	287	55.3	215	35.8
Coronary artery, atherosclerosis				
Marked	48	9.3	126	21.0
Moderate	136	26.2	203	33.8
None or slight	335	64.5	271	45.2
Myocardial infarct	33	6.4	91	15.2
Myocardial fibrosis	41	7.9	89	14.8
Cerebral infarct or hemorrhage †	17	3.3	58	9.7
No cardiac or cerebral lesion	432	83.2	373	62.2

* This group includes moderate consumers of alcohol as well as total abstainers.

† Brains were removed for study in only one half of alcoholic group and one third of nonalcoholic group, but these included almost all cases in which neurologic symptoms were manifest during life.

Other notable differences between the alcoholic and nonalcoholic groups are revealed in further analyses (table 3). Some of these are concerned in the development of atherosclerosis. For example, the relatively low incidence of terminal hypertension or lack of evidence of antecedent hypertension as suggested by the low incidence of cardiac hypertrophy in the alcoholic group may be an important factor. Although not enough persons with diabetes are included in either series to alter appreciably the percentages shown in table 1, this condition is rare in chronic alcoholism. This may be attributed largely to the shorter survival period, the lower incidence of obesity and the smaller number of women in the alcoholic group. There are no striking differences in body weight in the two groups, but obese and underweight persons are more numerous in the nonalcoholic series.

The relatively high incidence of active tuberculosis in the alcoholic groups is in keeping with the well known increase of susceptibility to infection seen in this condition. The data in table 3 suggest that persons with alcoholism are remarkably resistant to the development of malignant tumors. This is not entirely explained by the relatively young age at which persons with chronic alcoholism die. Of 203 alcoholic men, 55 years of age or older at death, 33, or 16.3 per cent, had malignant tumors at necropsy. In a similar age group of 336 nonalcoholic men, 99, or 29.5 per cent, had malignant growths. This finding will be reported on in detail elsewhere.

TABLE 2.—*Age Distribution of Cases in Alcoholic and Nonalcoholic Groups*

Sex	Age, Years	Alcoholic Group		Nonalcoholic Group	
		Number	Per Cent	Number	Per Cent
Male	35-44	85	20.1	32	7.4
	45-54	135	31.9	66	15.2
	55-64	134	31.7	138	31.8
	65-74	56	13.2	136	31.3
	75-84	13	3.1	55	12.7
	85 and over	..	...	7	1.6
Female	35-44	31	32.3	16	9.6
	45-54	40	41.7	28	16.9
	55-64	15	15.7	50	30.1
	65-74	8	8.3	42	25.3
	75-84	1	1.0	24	14.5
	85 and over	1	1.0	6	3.6

The 27.9 per cent incidence of cirrhosis in the alcoholic group is considerably higher than has been reported. Haggard and Jellinek,[15] for example, found only 8.7 per cent of persons with chronic alcoholism had cirrhosis at necropsy. In the present series, the analyses are limited to persons 35 years of age and older, and the cirrhotic group includes hepatic lesions of all degrees of severity, in many of which the evidence of cirrhosis was only noted on histologic study. This probably accounts for the relatively high incidence of this lesion not only in the alcoholic but also in the nonalcoholic group, although the severity of the criteria used in measuring excessive alcoholism may be an additional factor.

The association of cirrhosis with chronic alcoholism has little demonstrable influence on the incidence of atherosclerosis. The incidence of severe, moderate and mild generalized atherosclerosis is 8.3, 33.1 and 58.8 per cent respcctively in the alcoholic addicts with cirrhosis, and 14.4, 31.6 and 54.6 per cent in the alcoholic addicts without cirrhosis. Thus the incidence of moderate and mild degrees of atherosclerosis in the two categories is approximately the same. The higher incidence of severe atherosclerosis in the alcoholic addicts without cirrhosis is explained by the inclusion of a slightly larger percentage of old persons in this category. Fifteen and eight-tenths per cent of the persons without cirrhosis and 13.1 per cent of the persons with cirrhosis were over 65 years of age at death.

TABLE 3.—*Incidence of Coincidental Conditions in Alcoholic and Nonalcoholic Groups*

Condition	Alcoholic Group		Nonalcoholic Group	
	Number	Per Cent	Number	Per Cent
Hypertension	110	21.2	203	33.8
Cardiac hypertrophy	205	39.5	300	50.0
Diabetes mellitus	5	1.0	38	6.3
Obesity	82	15.8	126	21.0
Average weight	273	52.6	218	36.3
Underweight	164	31.6	256	42.7
Tuberculosis	58	11.2	30	5.0
Malignant tumor	43	8.3	156	26.0
Cirrhosis	145	27.9	40	6.7

In order to determine whether excessive alcoholism has a real rather than an apparent influence on the

15. Haggard and Jellinek,[14] p. 191.

TABLE 4.—*The Influence of Age on the Incidence of Atherosclerosis in Alcoholic and Nonalcoholic Men*

Lesion	Degree	Group	35-44 Years		45-54 Years		55-64 Years		65-74 Years		75 Years and Over	
			Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent
General atherosclerosis	Marked	Alcoholic	1	1.2	11	8.2	26	19.4	17	30.4	4	....
		Nonalcoholic	4	12.5	8	12.1	25	18.1	36	26.5	28	45.1
	Moderate	Alcoholic	15	17.6	43	31.8	53	39.6	25	44.7	7	....
		Nonalcoholic	3	9.4	25	37.9	56	40.6	63	46.3	23	37.1
	None or slight	Alcoholic	69	81.2	81	60.0	55	41.0	14	25.0	2	....
		Nonalcoholic	25	78.1	33	50.0	57	41.3	37	27.2	11	17.8
Coronary atherosclerosis	Marked	Alcoholic	3	3.5	8	5.9	15	11.2	15	26.8	2	....
		Nonalcoholic	4	12.5	6	9.1	29	21.0	36	26.5	20	32.3
	Moderate	Alcoholic	18	21.2	22	16.3	50	37.3	24	42.8	6	....
		Nonalcoholic	4	12.5	23	34.8	40	29.0	45	33.1	29	46.8
	None or slight	Alcoholic	64	75.3	105	77.8	69	51.5	17	30.4	5	....
		Nonalcoholic	24	75.0	37	56.1	69	50.0	55	40.4	13	20.9

TABLE 5.—*The Influence of Age on the Incidence of Atherosclerosis in Alcoholic and Nonalcoholic Men Without Hypertension or Cardiac Hypertrophy*

Lesion	Degree	Group	35-44 Years		45-54 Years		55-64 Years		65-74 Years		75 Years and Over	
			Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent
General atherosclerosis	Marked	Alcoholic	..	....	3	3.8	8	11.8	6	24.0	3	....
		Nonalcoholic	..	....	..	....	4	6.2	5	10.2	4	18.2
	Moderate	Alcoholic	4	8.5	27	34.2	26	38.2	10	40.0	6	....
		Nonalcoholic	2	11.8	7	28.0	21	32.3	22	44.9	12	54.5
	None or slight	Alcoholic	43	91.5	49	62.0	34	50.0	9	36.0	..	....
		Nonalcoholic	15	88.2	18	72.0	40	61.5	22	44.9	6	27.3
Coronary atherosclerosis	Marked	Alcoholic	1	2.1	2	2.5	3	4.4	1	4.0	1	....
		Nonalcoholic	..	....	..	....	5	7.7	5	10.2	4	18.2
	Moderate	Alcoholic	4	8.5	11	13.9	21	30.9	13	52.0	5	....
		Nonalcoholic	3	17.6	6	24.0	17	26.2	15	30.6	11	50.0
	None or slight	Alcoholic	42	89.4	66	83.6	44	64.7	11	44.0	3	....
		Nonalcoholic	14	82.4	19	76.0	43	66.1	29	59.2	7	31.8

TABLE 6.—*The Influence of Age on the Incidence of Atherosclerosis in Alcoholic and Nonalcoholic Men with Hypertension or Cardiac Hypertrophy*

Lesion	Degree	Group	35-44 Years		45-54 Years		55-64 Years		65-74 Years		75 Years and Over	
			Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent
General atherosclerosis	Marked	Alcoholic	1	2.6	8	14.3	18	27.3	11	35.5	1	....
		Nonalcoholic	4	....	8	19.5	21	28.8	31	35.6	24	60.0
	Moderate	Alcoholic	11	29.0	16	28.6	27	40.9	15	48.4	1	....
		Nonalcoholic	1	....	18	43.9	35	48.0	41	47.2	11	27.5
	None or slight	Alcoholic	26	68.4	32	57.1	21	31.8	5	16.1	2	....
		Nonalcoholic	10	....	15	36.6	17	23.2	15	17.2	5	12.5
Coronary atherosclerosis	Marked	Alcoholic	2	5.3	6	10.7	12	18.2	14	45.2	1	....
		Nonalcoholic	4	....	6	14.6	24	32.9	31	35.6	16	40.0
	Moderate	Alcoholic	14	36.8	11	19.7	29	44.0	11	35.5	1	....
		Nonalcoholic	1	....	17	41.5	23	31.5	30	34.5	18	45.0
	None or slight	Alcoholic	22	57.9	39	69.6	25	37.8	6	19.3	2	....
		Nonalcoholic	10	....	18	43.9	26	35.6	26	29.9	6	15.0

TABLE 7.—*The Influence of Age and Blood Pressure on the Incidence of Lesions Associated with Coronary and Cerebral Atherosclerosis in Alcoholic and Nonalcoholic Men*

Blood Pressure	Lesion	Group	35-44 Years		45-54 Years		55-64 Years		65-74 Years		75 Years and Over	
			Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent	Number	Per Cent
Without hypertension or cardiac hypertrophy	No lesion	Alcoholic	45	95.8	72	91.1	61	89.6	18	72.0	6	....
		Nonalcoholic	17	....	23	92.0	53	81.5	26	73.5	10	45.5
	Myocardial infarct	Alcoholic	..	....	2	2.5	5	7.4	..	....	..	....
		Nonalcoholic	..	....	1	4.0	5	7.7	4	8.2	1	4.6
	Myocardial fibrosis	Alcoholic	1	2.1	4	5.1	2	2.9	7	28.0	3	....
		Nonalcoholic	..	....	1	....	5	7.7	7	14.3	8	36.4
	Cerebral hemorrhage or infarct	Alcoholic	1	2.1	1	4.0	1	1.5	1	4.0	..	....
		Nonalcoholic	..	....	..	....	4	6.2	2	4.1	3	13.6
With hypertension or cardiac hypertrophy	No lesion	Alcoholic	33	86.9	43	76.8	47	71.2	16	51.6	4	....
		Nonalcoholic	12	....	25	61.0	35	47.9	42	48.3	14	35.0
	Myocardial infarct	Alcoholic	4	10.5	7	12.5	8	12.1	6	19.4	..	....
		Nonalcoholic	3	....	7	17.1	21	28.7	24	27.3	9	22.5
	Myocardial fibrosis	Alcoholic	1	2.6	5	8.9	8	12.1	5	16.1	..	....
		Nonalcoholic	..	....	4	9.7	8	10.9	17	19.3	13	32.5
	Cerebral hemorrhage or infarct	Alcoholic	..	....	2	3.6	3	4.6	4	12.9	..	....
		Nonalcoholic	..	....	5	12.2	10	13.7	5	5.8	7	17.5

incidence of atherosclerosis, it is necessary to compare groups of similar age, sex and blood pressure and to allow for differences in general nutrition. The small series of 96 alcoholic women cannot be divided into subgroups of sufficient size for such a comparison. Further analysis is therefore limited to the 423 alcoholic and 434 nonalcoholic men.

The incidence of various grades of atherosclerosis in the alcoholic and nonalcoholic men in each decade is, in many instances, almost identical (table 4). In the younger decades severe general and coronary atherosclerosis is somewhat more common in the nonalcoholic groups. However, in some decades a larger percentage of nonalcoholic persons than of alcoholic addicts have only slight atherosclerosis. The differences in the two groups when allowance is made for age are neither great enough nor consistent enough to indicate that chronic alcoholism has any pronounced effect on the incidence of atherosclerosis.

The nonalcoholic group in table 4 contains a relatively large number of cases with hypertension and cardiac hypertrophy. It is possible therefore that in chronic alcoholism without hypertension the incidence of atherosclerosis may actually be greater than in the control group without hypertension. To a certain extent this appears to be true (table 5). When those with evidence of hypertension are excluded from both series, the incidence of severe atherosclerosis in the alcoholic group exceeds that in the nonalcoholic group in most decades for both general and coronary atherosclerosis. The percentage with only slight atherosclerosis is roughly the same in both groups. Comparison of hypertensive, alcoholic men with hypertensive, nonalcoholic men (table 6) reveals, on the other hand, a higher incidence of severe atherosclerosis in the nonalcoholic group.

These differences can be explained by the distribution of obese and underweight persons in the hypertensive and nonhypertensive categories of both groups. Of the nonalcoholic, hypertensive men 24.6 per cent were obese, whereas of the alcoholic, hypertensive men only 19.8 per cent were overweight. Similarly, in the nonhypertensive groups, 73.5 per cent of the nonalcoholic but only 44.8 per cent of the alcoholic men were underweight.

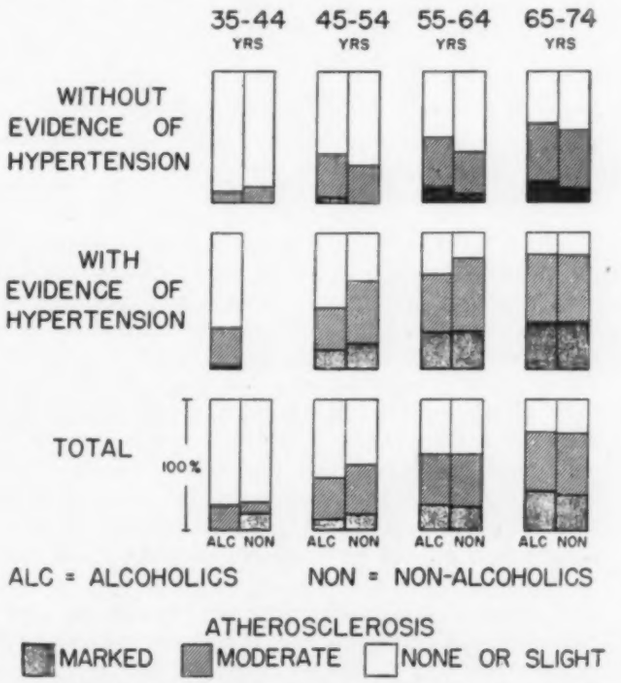
It may therefore be concluded that differences in incidence of atherosclerosis observed in alcoholic and nonalcoholic groups at necropsy are not the result of alcoholism per se but are attributable to associated differences in age, blood pressure and nutrition. Comparison of the incidence of atherosclerosis in the various categories of the two groups is shown graphically in the chart.

The low incidence of myocardial and cerebral lesions resulting from atherosclerosis in persons with chronic alcoholism may also be attributed to some extent to factors of age and blood pressure (table 7). This is particularly true in nonhypertensive groups, where it may be noted that about equal proportions of alcoholic and nonalcoholic men escape without cerebral or myocardial lesions. In the hypertensive group, however, both cerebral and cardiac lesions are somewhat more common in nonalcoholic persons than in persons with chronic alcoholism.

COMMENT

The principal fact that is disclosed by the foregoing analysis is that substitution of alcohol for a large portion of ordinary foods in the diet does not have, in itself, an appreciable effect on the development of atherosclerotic lesions. The apparent low incidence of atherosclerosis observed in chronic alcoholism is explained by (1) the relatively young age at death, (2) the low incidence of hypertension and (3) a lesser tendency for lesions in the heart and brain to develop, particularly in the presence of hypertension. Impressions concerning the incidence of atherosclerosis in chronic alcoholism based on casual observations are likely therefore to be quite erroneous.

The implication of this finding is that the materials deposited in atheromatous lesions are not necessarily derived as such from ingested food but that they may be elaborated within the body from other substances. In excessive alcoholism average body weight is usually maintained and the liver contains large amounts of fat. This suggests that much of the alcohol consumed may be converted into fat. Hyperlipemia, however, has not been described as a feature of chronic alcoholism.



Comparison of the incidence of generalized atherosclerosis in alcoholic and nonalcoholic men.

In acute alcoholism with damage to the liver, there is reduction of the cholesterol esters in the blood plasma according to Epstein and Greenspan.[16] These authors observed no significant change in blood cholesterol in persons with chronic alcoholism and cirrhosis. It is likely that enhancement or retardation of the development of atheromatous deposits depends more on fluctuations in the level of serum lipids than it does on the amount and character of lipids consumed.

SUMMARY AND CONCLUSION

The low incidence of atherosclerosis and associated lesions in chronic alcoholism depends on (1) the relatively young age at which persons with chronic alcoholism die and (2) the low incidence of association with conditions that favor the development of this disease such as hypertension, diabetes and obesity. It may be concluded, therefore, that substitution of alcohol for ordinary foods in the diet has no appreciable effect on the development of atherosclerosis.

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REACTIONS TO INTRAVENOUS ADMINISTRATION OF SOLUTIONS

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Despite the fact that many articles have appeared concerning the cause and elimination of pyrexial reactions after the administrations of solutions by vein, there still remains much lack of knowledge on the part of physicians and hospital personnel, so that these reactions still occur with a frequency inexcusable in the light of present day knowledge. Since most of the articles have appeared in technical or surgical journals they have escaped the eye of most of those responsible for the production of solutions and the care of tubing and needles, and therefore the application of the known successful methods of avoiding reactions has not become widespread. Commercial houses have, in general, attempted to correct the situation, but too often contact is made only with a purchasing agent who looks at the increased cost of material presented and refuses to buy it until forced to by the medical staff's complaints about reactions.

Seibert [1] in 1923 demonstrated that the substance responsible was the product of bacteria which exist in river water and in tap water. She proved that the material passed through the ordinary distilling apparatus but could be separated by spray-trapping devices.[1a] To this I added the principle of multiple baffle plates and deconcentrator tubes.[2] Triple distillation is not so effective in eliminating pyrogen, but will remove most of it. In 1932, following our publications many commercial firms began to prepare for sale pyrogen-free solutions. A biologic test was added—observation of leukocytes and temperature in rabbits after injection of test amounts intravenously, and therefore commercial houses now put out pyrogen-free solutions of all types. In hospitals where solutions are prepared by technicians and nurses this principle of proper distillation is often unknown or disregarded with disastrous results. Other methods have been devised, especially that of Co Tui [3] by adsorption filtration through asbestos filters, but none of these have become commercially applied.

The care of glassware and tubing remains the predominating factor in production of reactions. Those responsible for their care and preparation frequently know little of the facts, and often type of rubber and other factors are blamed which have nothing to do with the problem. The main fact is that tap water is the source of contamination, and any glassware or tubing rinsed or washed in tap water will produce pyrogen unless sterilized within an hour. Glassware in commercial houses is washed and sterilized simultaneously by use of steam jets. In hospitals it is too often simply rinsed, and distilled water and drugs are introduced into it and sterilized at the leisure of those concerned, which leads to gross contamination and production of pyrogen before sterilization is done. One must remember that bacteria themselves do not produce reaction, but their toxic products will do so. It has recently been demonstrated that the film of moisture within an ordinary intravenous needle can produce enough pyrogen to cause a reaction if grossly contaminated with tap water.

Similarly tubing rinsed with tap water and allowed to lie around in the laboratory will become contaminated in an hour's time. One may well wonder why all intravenous treatments are not attended by reactions if the principle of immediate sterilization after washing is not carried out, but one must remember that concentration of pyrogen-producing bacteria varies in various tap water and is increased if the water is stagnant in pipes for some time. Several commercial houses have attempted to prevent these tubing reactions by furnishing pyrogen-free disposable tubing, either cellophane or rubber, and as long as these are used with pyrogen-free solutions reactions can be eliminated. These sets are, however, rather expensive, especially when a great deal of solution is used. Pyrogen is readily soluble and can easily be washed out of tubing and glassware by simple distilled water—so that tubing, needle and glassware can be easily cleansed of it—but immediate sterilization must follow such preparation. The old method of boiling in sodium bicarbonate wastes time and does not eliminate all pyrogen and reactions.

Another frequent source of difficulty, if all these methods are followed by hospitals preparing their own solutions, is the accumulation of pyrogen in distilling apparatus. This factor produces sudden epidemics of reactions. In commercial preparation the need for cleaning apparatus is discovered by the biologic assay—Without this an arbitrary time for cleaning the apparatus must be set—at sufficiently frequent intervals to prevent these epidemics of reactions.

Much has been written concerning speed shock, and these writings are heeded to such an extent that interns and residents often introduce fluids so slowly that three to four hours are often used for one infusion. This causes great discomfort to the patient and often defeats the purpose for which the medication is given. Such slowly given fluids will not, for instance, correct hypochloremia if the patient loses more chloride from gastric drainage or vomiting than the infusion supplies. In all the intravenous solutions which I have seen administered, I have never seen speed shock if cardiac reserve is adequate. It is true that if pyrogen exists in solutions or tubing slow introduction may prevent a reaction if the concentration of pyrogen is low enough, but in pyrogen-free solutions administered through pyrogen-free sets, this should not be a factor.

Finally, if tubing or needles are suspected, the simple expedient of rinsing them and wasting 100 cc. or so of the solution will, because of the extreme solubility of pyrogen, prevent reaction if pyrogen-free solution is used. This was suggested by me in 1930,[4] and yet has received little attention.

SUMMARY AND CONCLUSIONS

Pyrogenic reactions from intravenous solutions remain a problem in many hospitals although the means to eliminate them entirely are well known. Immediate

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3. Co Tui and Wright, A. M.: The Preparation Non-Pyrogenic Infusion and Other Intravenous Fluids by Adsorptive Filtration: Report of Forty-Two Months' Trial, Ann. Surg. **116**: 412-425, 1942.

4. Rademaker, L. A.: Reactions After Intravenous Infusions: A Further Report on Their Elimination, Surg., Gynec. & Obst. **56**: 956-958, 1933.

sterilization after proper distillation will eliminate pyrogen from solutions, provided that glass containers are similarly sterilized after cleansing and rinsing with distilled water. Periodic cleansing of distilling apparatus is necessary. Immediate sterilization after rinsing with distilled water is necessary to prevent production of pyrogen in moisture films within tubing, needles and glassware. Use of disposable tubing and sets will eliminate reactions due to these factors. Cleansing of tubing just before administration of fluids by wasting 100 cc. or more of the solution and thus rinsing the apparatus will prevent reactions if nondisposable tubing is used, and is always a safety factor if there is doubt of the complete absence of pyrogen in tubing.

VAGUS NERVE SECTION (VAGOTOMY) IN THE TREATMENT OF PEPTIC ULCERS

Review of Literature and Report of Personal Cases

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Numerous theories have been propounded regarding the etiology of peptic ulcers; however, the recent and accurate observations of Dragstedt strongly suggest that an excess of unneutralized and undiluted gastric acid is a most important factor. Animal experimentation with Hiedenhain or Pavlov pouches demonstrates that pure gastric juice differs from gastric contents, in that the latter is a mixture of the former plus saliva, food, mucus, regurgitated duodenal juices and a neutral or faintly alkaline secretion from the pyloric antrum. Whereas pure gastric juice may be detrimental to living tissue, gastric contents are almost entirely inert. The effect of section of the vagus nerves on gastric secretion is not new. Brodie [1] in 1814 observed that the stomachs of dogs filled by intravenous injections of arsenic contained large amounts of mucus and watery fluid; if, however, the vagi were cut prior to the administration of arsenic the stomach remained empty. In 1870, Wood [2] confirmed these observations. Pavlov [3] in 1894 made similar observations on dogs and found that hydrochloric acid was not present after section of the vagus nerves. Further work by Pavlov [4] in 1910 emphasized the nervous or neurogenic factor in gastric secretion, which he thought could be completely abolished by vagus section. His deductions were only partially correct, since A. J. Carlson [5] has shown that although the nerve or neurogenic secretion was abolished there still existed a hormonal (humoral) secretion (gastrin), which is believed to be formed in the intestine and absorbed by the blood stream. When food is present in the stomach, this secretion is formed even though the vagi are cut. The amounts of secretion produced by neurogenic and hormonal stimulation are unknown. Ivy [6] (1925), Lim, Ivy and McCarthy [7] (1925) have made valuable contributions to this subject and have confirmed the work of Pavlov.

To review the voluminous literature which has accumulated on the ulcer problem is a herculean task; however, the more important milestones should be recorded. In 1909, Bickel [8] removed the duodenum in 2 dogs and reestablished continuity by means of a gastrojejunostomy. The bile and pancreatic ducts were implanted into the anterior abdominal wall. Four and one-half weeks later, an autopsy revealed that in 1 of the animals jejunal ulcers had developed, one of which had perforated, producing peritonitis and death. The rarity of spontaneous ulcer in the dog has been recognized by a number of investigators; [9] therefore dogs are usually chosen as the laboratory animals for these experiments.[10] In 1911, Exalto [11] noticed that no ulcers developed in dogs in which a gastroenterostomy was performed, but were frequently noted in those animals in which he did a Roux "Y" operation. He concluded that jejunal ulcers were due to the action of acid gastric juice on the intestinal mucosa. Mann and Williamson [12] described an operation in which the alkaline duodenal contents were shunted into the terminal ileum, and in 14 of 16 dogs on which they performed this procedure jejunal ulcers developed. This work gave the impetus for numerous other investigators who tried to determine whether it was bile, succus entericus or pancreatic juice which provided the protective neutralizing effect on gastric juice. Neuman, Demoor and Deloyers [13] found ulcers in 4 of 7 dogs who had a shunting of their bile into the terminal ileum, and Berg and Jobling [14] produced chronic duodenal ulcerations in 13 of 23 dogs after various types of biliary exclusions.

In 1931, Elman and Hartmann [15] produced ulcers in 6 dogs with pancreatic fistulas and emphasized the importance of pancreatic juice. Berg,[16] however, was able to produce only one ulcer in 16 dogs with pancreatic fistulas, and no ulcers after total pancreatectomy in 8 additional dogs. Kim and Ivy,[17] experimenting with neutral gastric mucin, noted spontaneous duodenal ulcers in 6 of 10 dogs with biliary fistulas.

Matthews and Dragstedt,[18] reviewing the work of Dragstedt and Vaughn,[19] emphasized the importance

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of the neutralizing effect of saliva, food, mucus and duodenal juices. Ochsner, Gage and Hosoi [20] were able to produce ulcers in 85 per cent of animals in which gastric pouches were anastomosed to the jejunum; however, if bile was introduced by anastomosing the gallbladder to this pouch, the incidence of ulcer dropped to 39 per cent. DeBakey [21] also attempted to answer the perplexing question, which had the greatest protective power, bile, pancreatic juice or succus entericus. He did this by performing gastrojejunostomies with von Eiselsberg [22] pyloric exclusions, and then excluded bile and pancreatic juice separately and collectively. He found that with pyloric exclusion alone ulcers developed in 50 per cent of the animals; with pancreatic juice excluded, 70 per cent; with bile excluded, 90 per cent, and with both juices excluded, 100 per cent. He concluded that bile is of the greatest importance in preventing formation of jejunal ulcer, pancreatic juice next and succus entericus least. In 1941, Varco, Code, Walpole and Wangensteen [23] produced increased gastric secretion and ulcers in dogs by intramuscular injection of a mixture of histamine and beeswax.

In 1925, McCrea,[24] after reviewing and studying the subject, came to the following conclusions: Unilateral vagotomy did not affect the motor activity of the stomach and bilateral vagotomy merely decreased the initial emptying time. Section of the vagi eliminated the psychic secretion, but the chemical phase of secretion still persisted. In 1929, Hartzell [25] reported that after transthoracic vagotomies on dogs complete section of the nerves induced a decrease in acid secretion, and that transabdominal vagus section showed no constant decrease in the height of acid. If the vagotomy was incomplete, no decrease in acid secretion resulted.

In 1930, Dragstedt and Ellis,[26] in an attempt to secure information concerning the relative importance of the vagus nerves in the secretion of gastric juice, performed an experiment with dogs in which they isolated the stomach (nerve and blood supply intact); intestinal continuity was made possible by an esophagojejunostomy. A gold-plated cannula placed in these stomachs collected the secretions. After eating, the isolated stomach secreted from 1,000 to 2,500 cc. of highly acid gastric juice in a twenty-four hour period. The animals would have to be kept alive by being supplied with chlorides, since they would "secrete themselves to death." In those dogs which were kept alive ulcers developed. If the vagi were cut, the acidity and amount of secretion immediately dropped to 300 to 600 cc. per twenty-four hours, and ulcers did not develop.[27] These theoretic considerations led Dragstedt to attempt section of the vagus nerves as a treatment for peptic ulcer.

In 1914, Exner and Schwarzmann [28] performed subdiaphragmatic resection of the vagus nerves in patients suffering with gastric crises, and by adding a gastrojejunostomy they attempted to avert the effects of atony, dilatation and pylorospasm. In 1920, Stierlin [29] was the first to suggest an operation on the nerve apparatus of the stomach for ulcer in human beings. His operation consisted of a circular incision through the muscularis and to the submucosa on the upper part of the corpus of the stomach; this incision was then sutured together. By this procedure, he proposed to cut the nerves, but Stierlin's circular myotomy failed because of an erroneous conception of the anatomy of the vagus nerves. Latarjet [30] in 1921-1922 devised an operation, vagotomy plus gastroenterostomy, in which he attempted to remove sensation, diminish the frequency and intensity of the contractions and diminish acidity. Schiassi,[31] in 1927, also attempted to cure ulcers by nerve section, and obtained favorable results in a group of 25 patients. Alvarez [32] (1928) lowered gastric acidity after experimental vagotomy.

In 1938, Winkelstein and Berg [33] reported that vagotomy alone or in combination with other surgical procedures seemed highly desirable in the therapy of peptic ulcer. In 1944, Weinstein, Colp and others,[34] while writing on vagotomy in the therapy of peptic ulcers, stated that "in none of the cases was cleancut evidence of beneficial therapeutic effect obtained."

In 1932, Cushing [35] stressed the importance of the part played by the central nervous system in the pathogenesis of ulcers. In this modern era of psychosomatic medicine, the factors of nervous tension, emotion, stress, strain, responsibility, competitive effort and frustration have all been emphasized. Winkelstein [36] has presented evidence that the hypersecretion of gastric juice in patients with ulcer is of nervous origin and that subphrenic section of the anterior vagus nerve together with partial gastrectomy or gastroenterostomy lessens recurrences of ulcers. The central nervous system may cause ulcers by producing a hypertonus in both the secretory and the motor fibers of the vagus; hence severing them seems logical. Both hypermotility and hypersecretion are abolished by complete section of the vagus fibers,[37] and the secretion and acidity tend to return to normal. Between meals, when there is no buffer action of food, hypersecretion and hyperacidity may prove dangerous. At the present time, Dragstedt [27] has obtained beneficial effects with vagotomy,

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and to date has reported no recurrences of ulcers; however, he stated that "a longer period of observation and a more extensive series of patients are obviously necessary to provide final answers."

ANATOMY

Successfully to correct hypersecretion and hypermotility, one must completely sever the vagus nerves, and to accomplish the latter it is necessary to have a thorough understanding of the anatomy. Unfortunately, there are marked contradictions in the leading textbooks on anatomy regarding the vagi. This is probably due to the fact that erroneous information was obtained from works by Hirschfeld and Leveillé [38] and Kollmann [39] in the middle of the nineteenth century, and many of the modern textbooks have obtained their information from these sources.

Probably the most reliable information comes from E. Perman,[40] who in 1935 performed a series of painstaking and accurate dissections dealing wth this subject. His conclusions are interesting, instructive and apparently accurate. He concluded that both vagi reach the stomach through the lesser omentum and that they divide into branches without the formation of a plexus of intertwining fibers. He stated that anastomoses exist between the various branches but that they do not lose their individuality as would be the case in a nerve plexus. The left vagus nerve sends branches to the liver and to the anterior wall of the stomach. Those traveling to the liver turn to the right, pass through the lesser omentum and to the porta hepatis. The gastric branches divide into several smaller nerves, which spread over the anterior wall and can be followed to the greater curvature. The right vagus nerve is arranged in a similar manner; one part to the celiac plexus, and the remainder supply the posterior wall of the stomach. Perman was unable to follow branches of either the left or right vagus into the greater omentum.

Recently papers have appeared dealing with the subject of the nerve supply to the stomach, but they too are quite contradictory. Bradley, Small, Wilson and Walters [41] examined 111 cadavers and concluded that there was a great variation in nerve pattern from the cardiopulmonary plexus to the stomach but that the nerves were very constant in course and distribution after reaching the stomach. They divided the nerve patterns into four groups. Miller and Davis [42] studied the vagus nerves below the level of the pulmonary plexus in 13 cadavers. They stated that in only 3 instances were the nerve arrangements comparable to those described in the textbooks as "normal" and that the remaining 10 showed marked variations. The picture is still in a state of confusion.

TRANSABDOMINAL VERSUS TRANSTHORACIC VAGUS NERVE SECTION (VAGOTOMY)

Walters and colleagues [41] stated that in 90 per cent of cases a transabdominal subdiaphragmatic approach will allow as nearly a complete division of the gastric nerves as the transthoracic route. Miller and Davis,[42] however, have expressed the opinion that the transthoracic approach is the one of choice.

Each of these approaches has its advantages and disadvantages. The transthoracic approach has the following advantages: (1) good exposure and (2) more complete sectioning of the nerves. Its disadvantages are: 1. The lesion cannot be examined (possible malignancy). 2. Pyloric obstruction cannot be corrected. 3. Postvagotomy gastric atony cannot be corrected. 4. Postoperative pain in the incision and costovertebral joint may result. 5. Gastroenterostomy is a difficult and unsatisfactory procedure when performed as a secondary operation on a dilated and atonic stomach. 6. Intrathoracic complications may result.

With these points in mind, it becomes apparent that each case will present a problem unto itself, and that it will be up to the surgeon's judgment and evaluation to decide which of the two approaches is preferable. For example: it is still a fact that every gastric ulcer is a potential malignant growth. Warren H. Cole [43] stated that gastric carcinoma is preceded in from 5 to 10 per cent of instances by an ulcer. Such lesions, therefore, should be exposed, removed and examined, whether or not vagus nerve section is performed. It would be a gross error to believe that one has done a complete bilateral vagus section only to learn later that some of the vagus fibers have remained intact and that a gastric carcinoma has developed. The transthoracic approach, on the other hand, is indicated for duodenal ulcers, especially if a previous gastroenterostomy has been done; this approach is also excellent for the anastomotic ulcer if it is deemed unnecessary to remove the ulcer. At present, the transabdominal route is favored for the reasons cited, and especially since a gastroenterostomy may be done simultaneously to compensate for the atony which may result after the section of the nerves. Such atony is not true paralysis, but may result in an acute dilatation of the stomach brought about by the release of the hypertonicity plus swallowed air, saliva and mucus. In my series, in 2 cases the transthoracic approach was used and in the remaining 23 the transabdominal.

SURGICAL TECHNIC

Transthoracic Vagotomy (fig. 1).—General anesthesia with positive pressure is used, and an incision is made over the seventh or eighth rib on the left side. A large section of the rib is resected, the pleural cavity entered, and after the inferior pulmonary ligament has been divided the left lung is retracted upward. Some prefer to enter the pleural cavity through an interspace rather than resect a rib. Recognition of the so-called esophageal triangle aids in rapidly locating the lower end of the esophagus. This triangle is bounded in front by the heart, behind by the descending aorta and below by the diaphragm (fig. 1 *D*). The pleura covering the triangle is incised and the esophagus identified and mobilized. The main vagus trunks are recognized by touch rather than sight. The nerves feel like taut cords which can readily be differentiated from the more yielding muscle of the esophagus The fibers are assembled by finger dissection into two main trunks, comprising the right and left vagi, which are ligated and divided. Some prefer to take a section of the nerve, but I have not done this routinely. In addition to the two trunks, small vagus fibers penetrate the esophageal wall; these must be combed off the esophagus and severed. The esophagus is replaced in its bed, the overlying

38. Hirschfeld, L., and Leveillé, J. B.: Névrologie, ou description et icongraphie du système nerveux et des organes des sens de l'homme, Paris, J. B. Baillière, 1853.

39. Kollmann, J.: Ueber den Verlauf d. Lungenmagennerven in der Bauchhohle, Ztschr. f. wissensch. Zool. **10**: 413-448, 1860.

40. Perman, E.: Surgical Treatment of Gastric and Duodenal Ulcer, Acta chir. Scandinav. (supp. 38) **77**: 1-35, 1935.

41. Bradley, W.; Small, J.; Wilson, J., and Walters, W.: Anatomic Considerations of Gastric Neurectomy, J. A. M. A. **133**: 459-461 (Feb. 15) 1947.

42. Miller, E., and Davis, C.: The Anatomic Study of the Vagus Nerves, J. A. M. A. **133**: 461-462 (Feb. 15) 1947.

43. Cole, W. H.: Surgical Aspects of the Peptic Ulcer, J. Missouri M. A. **3**: 474-477, 1939.

pleura sutured and the chest closed without drainage. The patients are encouraged to get out of bed the first or second postoperative day.

Transabdominal Vagotomy (fig. 2).—A long incision is necessary to obtain proper exposure. We utilize a muscle-splitting incision in the left rectus which commences in the angle between

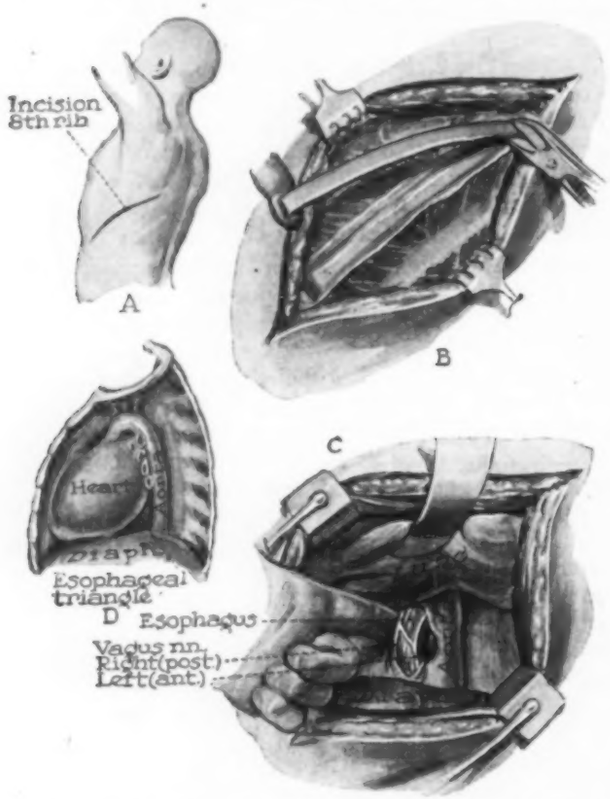

Fig. 1.—Transthoracic vagotomy. *A*, incision over the left eighth rib. *B*, removal of a section of the left eighth rib. Some prefer to enter the pleural cavity through an interspace rather than resect a rib. *C*, mobilization of the esophagus and exposure of the vagus nerves. A communicating nerve branch which is rather constant is noted in this subject. *D*, the esophageal triangle. The esophagus can readily be found in a triangle bounded in front by the heart, behind by the descending aorta and below by the diaphragm.

the xiphoid and left costal cartilage and extends 1 or 2 inches (2.5 or 5 cm.) below the umbilicus. The peritoneal cavity is entered and the left triangular ligament of the liver is exposed and made taut. This bloodless fold is incised, and it then becomes possible to retract the left lobe of the liver to the right. The peritoneum covering the lower end of the esophagus is incised and a finger or scissors are placed into the posterior mediastinum to mobilize the esophagus so that its lower 3 or 4 inches (7.6 or 10.2 cm.) can be delivered into the abdomen. The nerves are treated in much the same way as has been described in the transthoracic procedure; at times it is possible to isolate and ligate both vagi on the left side. I have observed that the left (anterior) vagus has a tendency to hug the esophagus and that the right (posterior) travels a slight distance away from it; therefore it is easier to feel and identify the latter. At the conclusion of the operation, the left lobe of the liver is permitted to fall into place; it has been found unnecessary to resuture the severed left triangular ligament. That this structure does not require suturing has been all too well revealed to me at a postmortem examination performed two weeks after sectioning of the vagus nerves (this case is reported in the section Personal Observations). The left lobe of the liver was found firmly fixed in place. An anterior gastroenterostomy is usually done after section of the vagus nerves. The suture material used in this entire series was spool cotton, the only exception being the use of surgical catgut in the through and through suture when a gastroenterostomy was performed.[44] These patients are placed on no postoperative dietary restrictions whatsoever, and early ambulation is encouraged.

POSTOPERATIVE COMPLICATIONS

A postoperative gastric atony, not paralysis, may result. Plus a vagus and sympathetic nerve supply, the stomach has a peripheral nerve supply which gives it an automatism. In general, vagus fibers are augmentors and the sympathetic fibers decrease tonus. Postvagotomy atony is believed to be due to a transient increased pyloric tonus; swallowed air and saliva may aggravate the condition so that an acute gastric dilatation results. To prevent this, constant Wangensteen suction is instituted for three to five days postoperatively. This is continued until all tendency toward nausea or vomiting is relieved. Certain medicaments, especially those of the choline group, show some promise in the treatment of gastric atony; time will prove their efficiency. A certain number of patients have a tendency to contract diarrhea, but this has not proved annoying and has been only transient. Two patients in my series stated that a resistant and annoying chronic constipation was completely relieved after vagotomy. Foul-smelling belching and emesis may result; I have not noticed these complaints.

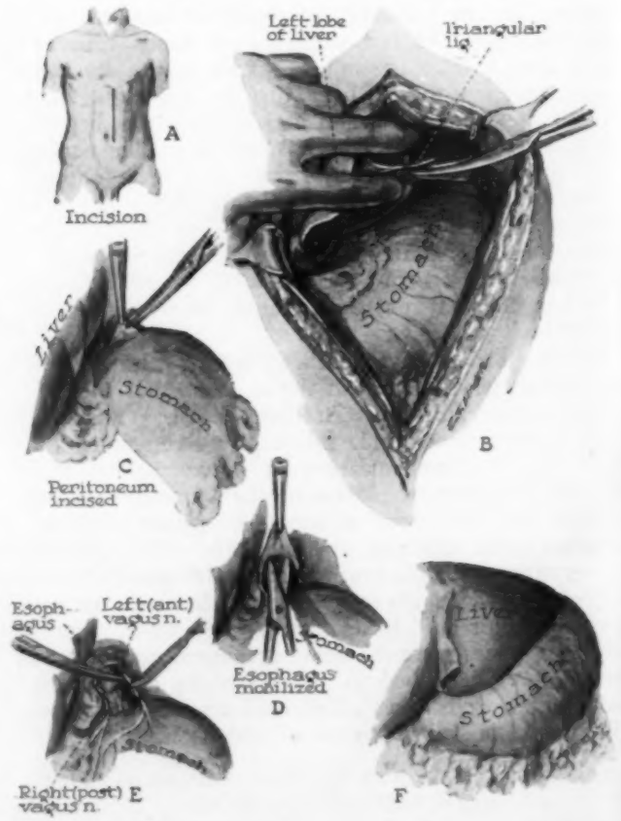

Fig. 2.—Transabdominal vagotomy. *A*, an incision in the left rectus extending from the angle between the xiphoid and the costal margin to an inch or 2 below the umbilicus. *B*, the left lobe of the liver is retracted to the right, rendering the left triangular ligament taut. This is incised, permitting dislocation of the left lobe of the liver. *C*, incising the peritoneum over the esophagus. *D*, mobilization of the esophagus from the posterior mediastinum into the abdomen. *E*, severing the vagi. *F*, replacing the left lobe of the liver.

In 1 of Dragstedt's patients a postvagotomy obstruction developed, which was thought to be due to the vagus nerve section. However, on reoperation by

44. Thorek, P.: Five Years Experience with Spool Cotton as a Suture Material, Am. J. Surg. **71**: 654-656, 1946.

Warren H. Cole,[45] this was found to be due to cicatricial stenosis caused by a healing ulcer.

To obtain complete relief and successful results, it is imperative that all vagus fibers be severed. Many tests have been devised to determine whether or not this has been accomplished, but the two most commonly used are the sham meal and insulin tests.[46] Since insulin shock complications are always a possibility with the insulin test, it is essential to have a physician present for the immediate administration of glucose.

That it is possible to overlook fibers of the vagus nerve seems to be agreed. Dragstedt stated that in his first 50 transthoracic vagus nerve sections, 3 incomplete vagotomies resulted. Hollander reported that in a series of 21 cases, 48 per cent proved to be incomplete with the insulin test.[47] It must be remembered, however, that gastroenterostomy or gastrectomy also reduces gastric acidity; hence, when these tests are performed in connection with vagotomy, it may be difficult to tell which procedure is responsible for the resulting achlorhydria.

PERSONAL OBSERVATIONS

I have performed 25 vagotomies in the past eighteen months; 3 deaths are recorded in this series, none of which can be directly attributed to the operative procedure. In the first of these patients gastric dilatation developed. This was believed to be due to the bilateral vagotomy, but postmortem examination revealed that the main trunk of the right (posterior) vagus was completely missed and remained intact. A massive lobar pneumonia of the left lung accounted for the death. The second death was in a patient who had a gastroenterostomy seventeen years prior to entrance. He entered with a diagnosis of a marginal ulcer. A degastroenterostomy was performed, followed by a subtotal gastric resection. Six weeks later he was readmitted to the hospital with violent pain. Exploration revealed three new acute jejunal anastomotic ulcers. A more radical resection was done, and transabdominal bilateral vagotomy added. He obtained immediate relief and left the hospital in two weeks. Seven weeks after the operation he was rushed to the hospital in a state of profound shock with signs of generalized peritonitis. He died, and postmortem examination revealed a ruptured jejunal ulcer. The third patient died forty-eight hours after a bilateral transabdominal vagus section and anterior gastrojejunostomy. Shortly after the operation a shocklike syndrome developed, from which condition she did not recover. Permission for autopsy could not be obtained; hence no conclusions can be drawn. When these 3 cases were analyzed, the immediate cause of death could not be said to be the vagus nerve section.

Weeks, Ryan and VanHoy[48] reported 2 deaths associated with supradiaphragmatic vagotomy, but since 1 of these was associated with a bilateral thoracolumbar sympathectomy, and the second patient had known methyl alcohol poisoning and at that had only the right vagus sectioned, it is difficult to see why the vagotomy per se should be blamed.

In my remaining 22 cases, the results have been most encouraging. It is indeed gratifying to note the immediate relief obtained after vagotomy and the ability of the patient again to enjoy a full meal and lead a normal life. Moore and co-workers[49] recently reported a series of 40 patients on whom he performed resection of the vagus nerves. The authors stated that their clinical results were good and that healing of the ulcer was the most uniform feature; transient undesirable side effects were found in about 10 per cent of the patients.

What the future holds for the functions of the liver, pancreas, kidney and intestinal tract following vagus nerve section cannot be stated at this time. Although these pros and cons cannot be definitely settled, the question should be approached and followed with an unbiased attitude. Whether or not the vagus nerves will regenerate can be proved only by careful follow-ups of these patients.

SUMMARY

The literature pertaining to vagotomy and peptic ulcer has been reviewed. A personal series of 25 cases is reported and 3 deaths in this series have been evaluated.

Whether the divided vagi will regenerate or whether permanent impaired gastric motility will result cannot be stated at this time.

The operation seems indicated in duodenal and stomal ulcers which do not respond to medical treatment. Gastric ulcers with their probable tendency toward malignant degeneration should be resected.

The transabdominal operation has distinct advantages in that the lesion may be inspected and a gastroenterostomy performed to compensate for obstructive or atonic complications.

Vagus nerve section may one day have a definite place in the therapy of peptic ulcers; however, the period of observation has been too short for final deductions.

ADDENDUM

Since submission of this article fifteen additional bilateral vagus nerve sections have been done with most encouraging results and no deaths. These were all done transabdominally and only two had gastrojejunostomies performed in addition.

850 West Irving Park Road (13).

45. Cole, W. H.: Personal communication to the author.
46. Thornton, T. F.; Storer, E. H., and Dragstedt, L. R.: Supradiaphragmatic Section of the Vagus Nerves, J. A. M. A. **130**: 764-771 (March 23) 1946.
47. Hollander, F.: The Insulin Test for the Presence of Intact Nerve Fibers After Vagal Operations for Peptic Ulcer, Gastroenterology **7**: 607-614, 1946.
48. Weeks, C.; Ryan, B. J., and VanHoy, J. M.: Two Deaths Associated with Supradiaphragmatic Vagotomy, J. A. M. A. **132**: 988-990 (Dec. 21) 1946.
49. Moore, F. D.; Chapman, W. P.; Schulz, M. D., and Jones, C. M.: Resection of the Vagus Nerves in Peptic Ulcer, J. A. M. A. **133**: 741-748 (March 15) 1947.

Epidemics of Virulent Smallpox.—During the period 1900 to 1929, epidemics of virulent smallpox were reported throughout the United States. Notable among these were the outbreaks in 1921 in Denver and Kansas City (Mo.), when the former city reported 924 cases and 37 deaths, and the latter 943 cases and 160 deaths. In 1924, Detroit reported 1,610 cases and 163 deaths. In 1901, an epidemic of smallpox in New York City resulted in 1,959 cases and 410 deaths. Had the same rate prevailed in the 1947 outbreak, there would have been 4,310 cases and 902 deaths.

All of the cases of smallpox that occurred in New York in April, 1947, were of the virulent type which usually had a fatality rate of 40 per cent in children and 20 per cent in adults. Because of the virulence of the disease and its high communicability, it is little short of remarkable that there were only 12 cases in the entire outbreak.—Weinstein, Israel, M.D., An Outbreak of Smallpox in New York City, *American Journal of Public Health*, November, 1947.

Special Article

CANCER OF THE BLADDER AND PROSTATE

CHARLES HUGGINS, M.D.
and
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Chicago

This article is the third of a series to be published by the American Medical Association in cooperation with the American Cancer Society. The series is designed to aid in the early diagnosis of cancer and thereby to gain more effective results in treatment. When complete, the series will be published in book form by the W. B. Saunders Company under the sponsorship of the American Medical Association and the American Cancer Society.

Cancers of the urinary bladder and prostate are the commonest tumors encountered in urologic practice. In an unreasonably large number of cases the tumors are far advanced at the time that treatment is commenced because of needless procrastination on the part of the physician or the patient. Evidently the patient is apt to minimize the symptoms of hematuria and vesical discomfort, and the family physician often provides palliative treatment before instituting a diagnosis. This apathy is unfortunate, because distinct progress has been made in the last decade in the clinical therapy of these lesions and the urologist has much to offer in special diagnosis and treatment.

The vesical and prostatic tumors are quite different. Generally speaking the tumors of the bladder infiltrate and prostatic cancers metastasize, the reason for the difference not being apparent at present.

CANCER OF THE BLADDER

The present discussion is based largely on two groups, each of 50 patients observed between 1941-1944 and 1944-1947, respectively; data on these groups indicate the changing emphasis in the treatment of tumors of the bladder serious enough to warrant hospitalization.

Surgical Pathology.—Most of the tumors of the bladder are primary in that organ, and the dictum of the early German pathologists is true in this special case, namely that organs frequently involved by primary neoplasms seldom become the seat of metastasis. The only secondary tumors of the bladder which we have encountered have been leukemic infiltration (2 instances), endometriosis (1 case) and direct involvement by extension of cancers of the bowel and uterus. Tumors of the kidney and ureter do not involve the bladder, with one important exception: papillary carcinoma of the renal pelvis often involves the ureter and bladder by direct extension and growth.

Sarcomas of the bladder are uncommon, and we have encountered the lesion only in children; leiomyoma of the bladder wall is a rare disease [1] which usually occurs at the neck of the bladder to obstruct urination in women. Practically, the tumors of the bladder are of epithelial origin.

From the clinical point of view 2 great classes of vesical tumors exist, and all modern treatment rests on this concept; these are the papillary tumors and the solid neoplasms. These groups merge imperceptibly, as Jewett and Blackman [2] have demonstrated, but in general a papillary lesion is less malignant than a solid cancer. Rather close observation has led us to believe that benign tumors of the bladder do not become transformed into malignant neoplasms with time; a neoplastic process seems to arise as either a simple or an infiltrating tumor in the bladder.

About 80 per cent of tumors encountered have a papillary component. The size of the pedicle is of prognostic significance; a papillary tumor with a slender pedicle is usually cured with ease while a lesion associated with a wide base often is accompanied by infiltration. The solid tumors are sessile and usually ulcerated (fig. 1), and the pattern of transitional epithelium is often preserved; usually there is some metaplasia to the squamous type of cancer. The most malignant tumors are undifferentiated as regards cell type. Further grading of tumors of the bladder beyond the elementary principles stated has not been particularly useful in our experience.

The classic distribution of tumors within the bladder was observed in this series; the lower part of the posterior wall of the bladder including the trigone is most apt to become malignant. In the present series the upper half of the bladder was involved in 22 per cent of the cases; 2 per cent of the tumors were in the anterior bladder mucosa and 76 per cent in the posterior-inferior quadrant. Ash [3] observed that in more than two thirds of 2,700 cases of tumors of the bladder the lesions were located on the posterior wall near the trigone and that tumors of the anterior portion of the bladder wall were uncommon.

Fig. 1.—Solid carcinoma of the bladder adjacent to and blocking the ureter on the right (arrow); toothpicks have been inserted in the ureters and prostatic urethra of this surgical specimen.

Because the vesical tumors commonly are located in a vulnerable position with respect to the neck of the bladder and the ureteral orifices, obstruction to emptying of the renal pelvis with hydronephrosis is frequently encountered. In fact an important cause of death in untreated vesical cancer is renal insufficiency from bilateral hydronephrosis. In our experience when metastasis occurs it has been always associated with

From the Department of Surgery, University of Chicago, the School of Medicine.

1. Grauer, T. P.: Leiomyoma of the Bladder, J. Urol. **40**: 594-597 (Nov.) 1938.

2. Jewett, H. J., and Blackman, S. S.: Infiltrating Carcinoma of the Bladder: Histologic Pattern and Degree of Cellular Differentiation in Ninety-Seven Autopsy Cases, J. Urol. **56**: 200-210 (Aug.) 1946.

3. Ash, J. E.: Epithelial Tumors of the Bladder, J. Urol. **44**: 135-145 (Aug.) 1940.

involvement of the periaortic lymph nodes; distant metastasis is exceptional.

Natural Course of Cancer of the Bladder.—The average duration of life in 33 untreated patients reported by Forber [4] was 18.8 months. Welch and Nathanson [5] in a series of 28 untreated patients observed that 14 died in fourteen months and 25 were dead at the end of five years. However, occasionally one observes patients with multiple papillary tumors of the bladder which have been present for from eighteen to thirty years.

Experimental Production of Vesical Tumors.—There is a high incidence of tumors in aniline dye workers, especially associated with exposure to benzidine and the naphthylamines. Evans [6] found in 83 cases that the tumor appeared after six to twenty years' exposure and that adequate preventive measures greatly reduced this occupational hazard. Gay [7] observed that the earliest dye lesion in the human bladder is a localized hyperemia followed by proliferation of the basement layer of endothelium. Vesical tumors were produced by Schar [8] in rabbits exposed to air containing naphthylamine and by Perlmann and Staehler,[9] who injected this compound subcutaneously. In dogs Hueper and associates [10] effected similar tumors by the feeding and subcutaneous injection of beta-naphthylamine after twenty to twenty-six months.

The great majority of patients with vesical tumors have had no intimate contact with these dyes, and tumors of the bladder were certainly frequent before synthetic chemistry was a factor. The 100 patients in this series were engaged in sixty-six occupations. Steele, Koch and Steiner [11] have reported the extraction with butyl alcohol of a carcinogenic factor from human urine, and it is probable that some cancer-producing substance excreted in the urine is an inciting agent. Further, the estrogens, which are well known as carcinogens, are urinary constituents of men and women.

Age and Sex.—Cancer of the bladder is about three times as common in men as in women. In the present series there were 77 males and 23 females, a sex incidence identical with that reported by Shivers and Henderson [12] and Ash.[3] The lesion is rare before 35 or after 80 years of age. The highest incidence is between 55 and 65 years. The involvement with respect to age is identical in both men and women (fig. 2).

Symptoms.—Blood in the urine is the commonest symptom of vesical cancer and, conversely, tumors of the bladder are the commonest cause of hematuria. Bloody urine was observed by 94 of the present 100 patients and was the initial symptom in 76 per cent of cases. It was of interest that the urine of all 6 persons who had not observed gross hematuria contained microscopic blood. The duration of the hematuria varied from one day to ten years. Hematuria may vary from a single episode of slight bleeding in a patient otherwise well to constant gross hematuria with clots.

Vesical discomfort (frequency of urination, urgency and pain on urination) occurred in 57 patients. A loss of weight was reported in 29 cases. No other symptoms were present in significant numbers.

Diagnosis.—Unfortunately physical examination furnishes no clue to the presence of an early vesical tumor. In the late stages there is often induration detectable on vaginal or rectal examination or on palpation of the suprapubic regions; under these circumstances the tumor is extremely far advanced.

The urine always contained red cells or excess numbers of leukocytes when a vesical tumor was present in this series; on 2 occasions the urine of these patients was normal but search several hours or days later revealed an increase of cells.

Neoplastic cells were found in the urine of 38 patients in this series. Often they were present in considerable number and with such a typical appearance as to make a staining procedure unnecessary. The staining technic of Papanicolaou and Marshall [13] was helpful occasionally. The cancer cells in urine arising from a vesical neoplasm have relatively an exceedingly large nucleus and little cytoplasm, and the nuclei at times are multiple.

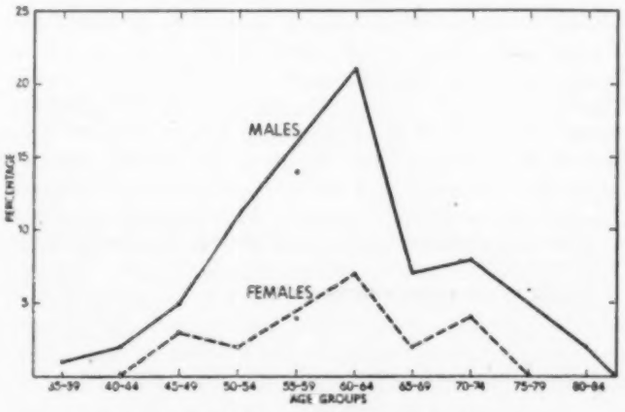

Fig. 2.—Distribution of bladder tumors in age groups.

Cystoscopic examination must always be undertaken when a patient has hematuria or a bladder tumor is suspected, and the bladder may be surveyed with a no. 16 F cystoscope generally without discomfort. The tumor is inspected with regard to location, size, relationship to the ureters, solidness or papillarity; the width of the pedicle, if any, is determined. Often fragments of the tumor appear in the irrigating fluid at cystoscopic examination, and these are examined in sections by means of routine histologic methods. Occasionally doubt arises in the interpretation of a lesion observed by cystoscopic means and a biopsy may be obtained with cystoscopic ronguer forceps or with the loop of a Stern-McCarthy resectoscope. Papillary tumors close to a ureter may be secondary to a carcinoma of the renal pelvis, so a lesion in this location requires retrograde pyelography.

Whenever a solid tumor of the urinary bladder is detected intravenous pyelography is carried out to determine the possibility of ureteral occlusion or dilatation;

4. Forber, J. E.: Incurable Cancer: An Investigation of Hospital Patients in Eastern London, Reports on Public Health and Medical Subjects, no. 66, Ministry of Health, London, His Majesty's Stationery Office, 1931.

5. Welch, C. E., and Nathanson, I. T.: Life Expectancy and Incidence of Malignant Disease: Carcinoma of Genitourinary Tract, Am. J. Cancer **31**: 586-597 (Dec.) 1937.

6. Evans, E. E.: Causative Agents and Protective Measures in the Anilin Tumor of the Bladder, J. Urol. **38**: 212-215 (Aug.) 1937.

7. Gay, D. M.: Pathology of Anilin Tumor of the Bladder, J. Urol. **38**: 221-231 (Aug.) 1937.

8. Schar, W.: Experimentelle Erzeugung von Blasentumoren: Die Wirkung langdauernder Inhalation von aromatischen Amidoverbindungen, Deutsche Ztschr. f. Chir. **226**: 81-97 (July) 1930.

9. Perlmann, S., and Staehler, W.: Ueber künstlich erzeugte Geschwülste der Blase, Klin. Wchnschr. **11**: 1955-1956 (Nov.) 1932.

10. Hueper, W. C.; Wiley, F. H., and Wolfe, H. D.: Experimental Production of Bladder Tumors in Dogs by Administration of Beta-Naphthylamine, J. Indust. Hyg. **20**: 46-84 (Jan.) 1938.

11. Steele, R.; Koch, F. C., and Steiner, P. E.: The Extraction of a Carcinogenic Fraction from Human Urine, Cancer Research **1**: 614-617 (Aug.) 1941.

12. Shivers, C. H. de T., and Henderson, K. P.: Tumors of the Bladder: A Review of One Hundred and One Cases, J. Urol. **42**: 761-777 (Nov.) 1939.

13. Papanicolaou, G. N., and Marshall, V. F.: Urine Sediment Smears as a Diagnostic Procedure in Cancer of the Urinary Tract, Science **101**: 519-520 (May 18) 1945.

these changes are often silent and are of obvious importance in treatment. In this series unilateral ureteral obstruction by tumor occurred in 13 cases.

Treatment.—Only two methods of treatment are available, surgery and radiation. Radiation has been used extensively by many clinicians and was highly developed by B. S. Barringer,[14] but the use of radiant energy through radium or radon seems to be declining rapidly in this country. The implantation of radium or radon needles in the bladder has been followed in many patients by prolonged cystitis. In Barringer's series there were 24.1 per cent of five year cures; Marshall [15] reported that 6 per cent of radiation-treated patients were free from tumor at the end of five years. It is certain that a small number of vesical tumors are radiation-sensitive, but most of them are insensitive except to unreasonably large amounts of these agents. Ash[8] has stated an opinion which is held by many urologists—"It seems very doubtful that any case that could be cured by irradiation could not be cured by skillful surgery. . . ."

It is impossible at this time to give rigid specifications for the surgical treatment of all cases of vesical tumor; clearly the treatment must always be individualized to suit any particular case. In general the surgical plan used in this clinic depends on the size, number and papillomatous nature of the tumors. (*a*) Papillary tumors which are small in size and few in number are treated by endoscopic fulguration with a Bugbee electrode. This treatment is carried out on ambulatory patients, and none of these cases has been included in the present series. (*b*) Papillary tumors of large size but with a narrow pedicle are treated by transurethral resection with a Stern-McCarthy resectoscope. (*c*) Papillary tumors with a broad base are examined by an exploratory suprapubic cystotomy; when the lesion apparently is not infiltrating the lesion is fulgurated with diathermy at open operation or excised by segmental resection, provided the tumor can be removed with a wide cuff of normal bladder tissue. (*d*) Massive involvement of the bladder by small papillomas is treated by cystectomy.

Unless metastasis or local infiltration is present solid tumors are treated by cystectomy preceded by a deviation of the urinary stream, usually by bilateral ureterosigmoidostomy. Bilateral cutaneous ureterostomy or nephrostomy is not performed, since it is our belief that the care of two appliances presents insuperable difficulty for most patients. When ureterosigmoidostomy is not feasible because of obesity of the patient or exceptionally high grade ureteral dilatation, cutaneous ureterostomy with contralateral ligation of the ureter is performed according to the method of Huggins and Scott.[16]

Within the past three years the tendency in the treatment of vesical tumors has been toward more extensive surgical procedures; total cystectomy has been the operation carried out in 34 per cent of the later group of cases as compared with 12 per cent of the earlier series, and this has been at the expense of suprapubic fulguration. Partial resection has increased from 12 to 18 per cent of the total cases. Palliative permanent suprapubic cystotomy has been discontinued, being replaced in the hopeless cases by an internal or external ureteral shunt.

Ureteral transplantation tc the colon may be performed by an intraperitoneal method, or the sigmoid may be sutured to the peritoneum in the right and left lower quadrants of the abdomen and the anastomosis made extraperitoneally. The choice of the operation largely depends on the personal preference of the surgeon; the great advantage of the extraperitoneal technic is that leakage is not followed by peritonitis. This is not an undue risk, however, in the intraperitoneal operation, which has the great superiority that the ureter may be regularly transplanted without kinking or tension. In many technics the ureter is implanted obliquely through the wall of the colon; our results have improved considerably since this valve-producing procedure was abandoned, because it had no practical advantage and was conducive to the dreaded postoperative ureteral stricture.

Bilateral transplantation of the ureters in this series was done in a single stage operation, and our preference is for a sequestered intraperitoneal procedure. Preoperative preparation is important; intestinal antiseptics are administred to reduce the bacterial flora and the colon is emptied completely before the transplantation. The patient is placed on a liquid diet for forty-eight hours before the operation and 2 Gm. of succinylsulfathiazole is administered every two hours during the day. Saline enemas are given in the evening and morning before operation.

We consider profound relaxation of the abdominal wall to be important. Continuous spinal anesthesia is induced and a rectal tube is then passed to insure the absence of liquid in the colon. A midline incision is made from the umbilicus to the symphysis pubis and the peritoneal cavity is opened. The peritoneum is incised over the ureters, and these are amputated low in the pelvis. Through an incision not more than 1.5 cm. in length in the serosa of the sigmoid, a small opening is made into the lumen of the bowel and the ureter is guided by a suture into the colon. The incision in the bowel is closed loosely by several silk sutures, and the posterior peritoneal leaf representing the free margins of the incision used to mobilize the ureter is drawn up and sutured over the anastomosis, thus exteriorizing it. Tunneling of the ureter in the bowel is strictly avoided, and catheters are not used in the bowel. Feeding is begun as is tolerated by the patient on the day of operation. Penicillin 300,000 units daily is injected intramuscularly for five days. The patient arises from bed the day after transplantation. This procedure is brief, simple and practically bloodless, and cystectomy may frequently be performed at the same session.

Mortality.—The hospital deaths following open surgical procedures were 5.7 per cent in the series reported by Priestley,[17] which is essentially the same as that found by us. (See the accompanying table.) The operation of total cystectomy is in line with modern surgical thought wherein malignant lesions are widely excised, and ureterosigmoidostomy renders this possible. No extensive series of late follow-up results of cystectomy has been reported to date.

14. Barringer, B. S.: Radium Therapy of Bladder Carcinoma: Five Year Results; Failures; Future Therapy, J. Urol. **40**: 606-611 (Nov.) 1938.
15. Marshall, V. F.: A Comparison of Radiation and Surgery for Cancer of the Bladder, J. A. M. A. **134**: 501-507 (June 7) 1947.
16. Huggins, C., and Scott, W. W.: Cutaneous Ureterostomy with Contra-Lateral Ureteral Ligation, J. Urol. **53**: 325-338 (Feb.) 1945.
17. Priestley, J. T.: The Surgical Treatment of Carcinoma of the Bladder, J. A. M. A. **134**: 507-511 (June 7) 1947.

CANCER OF THE PROSTATE

The recognition of cancer of the prostate has become a matter of clinicial importance, since methods exist by which the disease can often be alleviated and controlled even when the tumor is far advanced and has metastasized. The diagnosis of cancer of the prostate has been enhanced also by recent developments whereby, under certain conditions, the diagnosis may be established by laboratory examination of the blood serum.

It is well to bear in mind that cancer of the prostate is a common disease, since it is the cause of death of about 5 per cent of white men over 50 years of age. Usually the lesion is far advanced when the patient is first seen by the urologist.

Surgical Pathology.—Geraghty and Boyd, as reported by Lowsley,[18] observed in 1912 that cancer of the prostate usually arises in the posterior region of

Fig. 3.—Human prostate excised for early carcinoma; the lesion is in the posterior lobe on the left.

the gland. This anatomic predilection (fig. 3) has been noticed by us repeatedly. Prostatic cancer rarely ulcerates through the rectovesical fascia into the rectum but frequently extends into the bladder in the trigone. The tumor spreads along the surface of the seminal vesicle and infiltrates the perineural lymphatics.[19] The metastases flourish in bone marrow and lymph nodes, while on the contrary the lung, spleen and brain are seldom involved.

The prostatic cancers most commonly encountered consist either of undifferentiated sheets of cells or of adenocarcinomas wherein tiny glands are reproduced. The essential criteria for pathologic diagnosis of cancer of the prostate are anaplasia and invasion. In adenocarcinoma the small irregular acini are closely packed and the normal, formal relationship to the fibromuscular stroma is lost.

Horning[20] has recently produced glandular carcinomas in the prostate of the Strong A strain of mice and has found that these tumors are transplantable in other mice; these important experiments represent the first successful production of prostatic adenocarcinoma in animals.

TABLE 1.—*Malignant Lesions of the Bladder*

Incidence and Mortality of Operations (1941-1947) in 100 Patients

Type of Operation	Total Operations	Hospital Deaths
Cutaneous ureterostomy	9	2
Bilateral ureterosigmoidostomy	20	1
Transurethral fulguration	44	0
Suprapubic fulguration	25	0
Partial cystectomy	15	0
Total cystectomy	23	1
Number of operations	136	..
Total deaths	...	4

The History.—A typical history in a case of prostatic cancer is that a man over 50 years of age has an increased frequency and some difficulty on urination with pain in the lower part of the back and loss of weight, the symptoms being of a few months' duration.

The disease is uncommon in men under the age of 50 (fig. 4). The symptoms may be absent but are often typical and usually become severe. They depend on interference with urination by the primary tumor; on the metastasis which usually occurs to bones and regional lymph nodes, and on the cachexia of carcinoma. The local symptoms from the prostate are increased urinary frequency (86 per cent)[21] and decreased size of the urinary stream (78 per cent), which leads to acute urinary retention (28 per cent); hematuria is uncommon (8 per cent). The osseous metastases produce pain, usually sciatica or lumbar backache (56 per cent) or pain in other regions where the bones are involved (14 per cent); these pains are often severe enough to require morphine injections. Certainly the onset of sciatica in a man over 40 years of age demands a rectal examination. Involvement of the regional

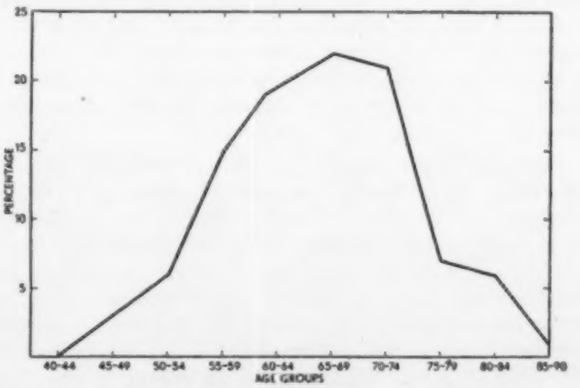

Fig. 4.—Distribution of prostatic cancer in age groups.

lymph nodes produces edema of the legs or genitalia (4 per cent). The symptoms usually extend over a short period, often months, usually less than a year when

18. Lowsley, O. S.: The Development of the Human Prostate Gland with Reference to the Development of Other Structures at the Neck of the Urinary Bladder, Am. J. Anat. **13**: 299-349, 1912.

19. Warren, S.; Harris, P. N., and Graves, R. C.: Osseous Metastasis of Carcinoma of the Prostate with Special Reference to the Perineural Lymphatics, Arch. Path. **22**: 139-160 (Aug.) 1936.

20. Horning, E. S.: Induction of Glandular Carcinomas of the Prostate in the Mouse, Lancet **2**: 829-830 (Dec. 7) 1946.

21. These data represent the incidence of symptoms in 50 consecutive clinical cases. Huggins, C.: The Diagnosis of Cancer of the Prostate Including the Interpretation of Serum Phosphatase Values, Bull. New York Acad. Med. **19**: 195-200 (March) 1943.

the patient is first seen; the patient with benign prostatic hypertrophy usually has complaints extending over a period of years.

Physical Observations.—The characteristic observations are apparent on rectal examination and consist of a hard nodular lumpy prostate—in early cancer a single hard lump, in later stages of disease multiple nodules with extension along the seminal vesicles and lateral to the prostate. In advanced prostatic cancer no clear line of demarcation exists between the prostate and the surrounding tissues such as always exists in benign prostatism.

Involvement of Virchow's supraclavicular node often occurs in prostatic cancer.

Nodular involvement of the prostate is occasionally found in the absence of carcinoma; such nodules have been caused by benign prostatic hypertrophy, prostatic calculi, tuberculosis and nonspecific prostatitis. A roentgen examination of the pelvis will reveal prostatic stones.

Roentgenologic Examination.—In a series of 50 patients with advanced prostatic cancer, roentgenologic evidence of osseous metastasis was observed in 31 cases. Both osteoblastic and osteolytic lesions were found; usually they occur together. Only in 2 cases were osteolytic lesions encountered without associated increased formation of bone; these lesions were small and multiple compared with the large melting away process commonly observed in hypernephroma. The pelvis was always involved when metastases had occurred in the bones, and lesions were never encountered distal to the knee or elbow. While other bones are often involved, roentgen examination of the pelvis alone is regarded as adequate in the routine clinical search for metastases; certainly filming of the long bones is usually a clear waste of resources.

The most puzzling condition in the roentgen diagnosis of prostatic metastases in bone occurs with Paget's disease (osteitis deformans). The fundamental roentgenologic evidence of Paget's disease is increased size of trabeculae, which are commonly wavy, plus cyst formation. In prostatic cancer the trabeculae of bone disappear, incorporated in dense osteosclerotic masses. Examination of the serum for acid and alkaline phosphatase activity is of particular importance when doubt exists concerning Paget's disease or prostatic cancer; in both states alkaline phosphatase is increased in activity, but only in prostatic cancer is acid phosphatase elevated.

Cystoscopic Examination.—When prostatic cancer is associated with benign prostatic hypertrophy, as not infrequently occurs, only the benign lesion is visible at cystoscopic examination. Unaccompanied by hypertrophy, advanced prostatic cancer often displays suggestive features, such as constriction of the posterior part of the urethra and infiltration of the trigone. A common sign is the appearance of small irregular notches around the vesical neck, compared with the notches found in prostatic hypertrophy which resemble formal architectural figures, Gothic in type.

Serologic Diagnosis.—This important diagnostic procedure was developed by A. B. and E. B. Gutman,[22] of Columbia University, and Barringer and Woodard,[23] of Memorial Hospital, independently in 1938 and depends on the important discovery of Gutman, Sproul and Gutman[24] (1936) that prostatic cancer contains large amounts of acid phosphatase. In brief, there exist two distinct enzymes, acid and alkaline phosphatase, which are capable of dephosphorylating monophosphoric esters to form inorganic phosphate. Alkaline phosphatase is particularly rich in concentration in the osteoblasts, and when there is brisk osteoblastic activity the value of this enzyme is increased in the blood serum; such states include rapid growth in children, Paget's disease, osteogenic sarcoma and osteoblastic metastasis from prostatic cancer. This enzyme is also increased in disease of the liver, in which it is an exquisite indicator of hepatic function. As far as is known, bone activity and hepatopathy are the only conditions in which the serum values are increased.

Acid phosphatase values of serum are significantly elevated only in cancer of the prostate, and in this condition only when metastasis has occurred. When prostatic cancer is located in bone marrow or lymph nodes, the secretions of these cells find their way into the blood plasma and, the enzymes being proteins, are not readily disposed of; hence, the acid phosphatase value increases above normal. In our laboratory the King and Armstrong method, with appropriate buffering, is used for determination of both enzymes; the normal values are: for acid phosphatase, less than 4.5 units, and for alkaline phosphatase, less than 12.5 units each per hundred cubic centimeters of serum. In a series of 100 cases of advanced prostatic cancer before treatment, one or both of the phosphatases were increased in 52 per cent and both were in the normal range in 48 per cent; with osteolytic metastasis alone the phosphatase values were never increased. Usually when there is an elevation of phosphatases both values are increased; however, in 1 case the acid value alone was high and in 5 cases only the alkaline phosphatase reading was elevated. When the serum acid phosphatase is significantly raised (greater than 10 units) it is certain that the patient has prostatic cancer with metastasis; values between 5 and 10 units are presumptive of prostatic cancer but are occasionally observed in other conditions. Patients frequently have advanced prostatic cancer even with metastasis to the bones accompanied with serum phosphatase levels in the normal range, but if both phosphatases are distinctly increased the diagnosis is established that cancer of the prostate with osteosclerotic osseous metastasis is present; there are false negatives, but no false positives. These tests are of special value when roentgenograms of the bones show equivocal changes. It is obviously necessary to determine both the phosphatases for maximum efficiency in diagnosis and prognosis of cancer of the prostate; these tests are as clearly necessary as studies of basal metabolism in thyroid disease.

Kearns[25] has also demonstrated a striking decrease in the sedimentation rate of the blood after the administration of estrogen.

Biopsy.—It is occasionally necessary to resort to biopsy to make the diagnosis of cancer of the prostate,

22. Gutman, A. B., and Gutman, E. B.: "Acid" Phosphatase and Functional Activity of the Prostate (Man) and Preputial Glands (Rat), Proc. Soc. Exper. Biol. & Med. **39**: 529-532 (Dec.) 1938; An "Acid" Phosphatase Occurring in the Serum of Patients with Metastasizing Carcinoma of the Prostate Gland, J. Clin. Investigation **17**: 473-478 (July) 1938; Adult Phosphatase Levels in Prepubertal Rhesus Prostate Tissue After Testosterone Propionate, Proc. Soc. Exper. Biol. & Med. **41**: 277-281 (May) 1939.

23. Barringer, B. S., and Woodard, H. Q.: Prostatic Carcinoma with Extensive Intra-Prostatic Calcification, with Discussion of Possible Role to Prostatic Phosphatase, Tr. Am. A. Genito-Urin. Surgeons **31**: 363-369 (May) 1938.

24. Gutman, E. B.; Sproul, E. E., and Gutman, A. B.: Significance of Increased Phosphatase Activity of Bone at Site of Osteoplastic Metastases Secondary to Carcinoma of Prostate Gland, Am. J. Cancer **28**: 485-494 (Nov.) 1936.

25. Kearns, W. M.: Treatment of Carcinoma of the Prostate with Estrogens, Wisconsin M. J. **41**: 575-581 (July) 1942.

and several methods exist for obtaining tissue. When prostatic cancer is suspected and the lesion is small, the perineal approach with removal of a section of the gland is best done, so that radical perineal prostatectomy can be carried out if the diagnosis is confirmed. When there is urinary obstruction in suspected advanced cancer, transurethral resection of the gland should be done so that the obstruction may be effectively removed in addition to obtaining tissue for pathologic examination.

In the differentiation of carcinoma arising in the prostate from vesical carcinoma or other malignant disease in this region (e. g. sarcoma of the prostate), valuable aid is often obtained by staining the tissue for acid phosphatase by the method of Gomori,[26] since prostatic epithelium contains much larger amounts of this enzyme than do other tissues. The tissue requires special fixation (in cold acetone) preliminary to staining for the site of enzymatic action.

The Treatment of Prostatic Cancer.—(*a*) Surgical: It is obvious that cancer is safer when it is in a bottle than in a patient. In early cancer of the prostate total excision of the gland through a perineal approach should be performed. This operation was developed by H. H. Young[27] and has been improved by many urologists, especially Elmer Belt,[28] so that it is no longer an operation of formidable proportions. Unfortunately, early cancer of this gland is not often seen clinically; in 138 consecutive cases of prostatic cancer seen in this clinic, only 2 were considered to be sufficiently early and confined that radical prostatectomy could be performed.

(*b*) Endocrine: The antiandrogenic treatment of cancer of the prostate was introduced from this clinic[29] and has proved to have both theoretical and practical significance. There emerged the fact that this cancer is usually not autonomous, since it shrinks or grows when androgens are administered or eliminated. The antiandrogenic measures have a general modality of action and were the first chemotherapeutic agents of known chemical constitution, aside from radium, of value against carcinoma.

Modification of the hormonal status of the patient as a form of treatment of prostatic cancer depends on the concept that most of these carcinomas are not tumors of embryonic or other primitive tissue but are neoplasms of sufficiently mature tissue that they are activated by androgens. In brief, cancer of the prostate is stimulated by injection of male sex hormones (androgens) and is inhibited by reduction of androgens either through excision of both testes or by neutralization through administration of female sex hormone (estrogen). By frequent observation of the serum phosphatase levels it was found that decreasing the amount or the activity of the androgens by castration or by administration of estrogen (diethylstilbestrol, 5 mg. daily) often caused a decrease of serum acid phosphatase values to or toward normal, whereas injection of androgen (testosterone propionate, 25 mg. daily) caused exacerbations of these phosphatase values and of the disease.

Certain benefits usually follow orchiectomy. Among the earliest changes are an increased appetite and relief of pain. These effects are often seen within several days following castration. They result in a gain in weight and an improvement in the anemia. Frequently there is a decrease of the primary tumor so that the hard, nodular, craggy prostate becomes smooth and soft and decreases appreciably in size. Changes often occur in the bony metastases on roentgen examination, with the metastatic lesions usually undergoing increased calcification within several months after orchiectomy. This increased density is often followed by a stabilization in growth or by disappearance of the metastases on roentgen examination. Other objective evidence of improvement that occurred in this series included the disappearance in 2 cases of paralysis due to compression from metastasis in the central nervous system and, in 2 other cases, the disappearance of enlarged lymph nodes on the site of metastases.

Certain undesirable symptoms also occur, notably abolition of the adult sexual capacity and the onset of hot flushes similar to menopausal changes in women, and which likewise can be mitigated by the administration of estrogen (diethylstilbestrol, 5 mg. daily by mouth for two weeks).

All in all, the improvement which occurs after orchiectomy in cancer of the prostate far outweighs the undesirable effects. It should be emphasized, however, that the results are not uniformly successful. Remissions of varying length of time occurred in 18 patients among 20 with disseminated prostatic cancer treated by orchiectomy while in 2 cases the cause of the disease was unmodified by the treatment. After five years, one patient was alive with slowly advancing carcinoma and in 4 patients there was no clinical or laboratory evidence of cancer; these results have not been changed at the present time, six and one-half and eight years after orchiectomy.

The question of inactivation of androgens by estrogens in prostatic cancer as opposed to castration naturally arises. There is a place for both methods of reducing the activity of the androgens. Endocrine castration with diethylstilbestrol (this estrogen is potent and as well tolerated as any other estrogen) is at first glance attractive, since it can be carried out without surgical intervention and is financially economical. For most patients, however, it is less efficient than castration for the several reasons which follow: The inhibition of androgens by estrogens is not complete, and a complete inhibition or elimination of androgens is the basis for the modern treatment of prostatic cancer. Moreover, this partial inhibition is temporary and the estrogen must be administered for long periods of time. A few patients do not tolerate estrogens well (pain in breasts and testes, digestive disturbances and the like). Furthermore, in many species the administration of estrogen to males for an extended length of time is in itself carcinogenic. While it was first shown in this laboratory that beneficial results occur in prostatic cancer both from surgical castration and estrogenic administration, we consider bilateral orchiectomy the method of choice for most patients as a basic treatment in advanced or metastatic cancer of the prostate. Aside from the relief of postorchiectomy hot flushes, chemical castration by estrogen treatment is indicated (1) when the patient refuses surgical castration (this has never happened in

26. Gomori, G.: Microtechnical Demonstration of Phosphatase in Tissue Sections, Proc. Soc. Exper. Biol. & Med. **42**: 23-26 (Oct.) 1939; Distribution of Acid Phosphatase in the Tissues Under Normal and Under Pathologic Conditions, Arch. Path. **32**: 189-199 (Aug.) 1941.

27. Young, H. H.: Early Diagnosis and Radical Cure of Carcinoma of Prostate: Being a Study of Forty Cases and Presentation of Radical Operation Which Was Carried Out in Four Cases, and an Appendix Compiled Later, Containing Complete Histories of Sixty-Four Cases, Bull. Johns Hopkins Hosp. **14**: 485-628, 1906.

28. Belt, E.: Radical Perineal Prostatectomy in Early Carcinoma of the Prostate, J. Urol. **48**: 287-297 (Sept.) 1942.

29. Huggins, C., and Hodges, C. V.: Studies on Prostatic Cancer: I. The Effect of Castration, of Estrogen and of Androgen Injection on Serum Phosphatase in Metastatic Carcinoma of the Prostate, Cancer Research **1**: 293-297 (April) 1941. Huggins, C.; Stevens, R. E., Jr., and Hodges, C. V.: Studies on Prostatic Cancer: I. The Effect of Castration on Advanced Carcinoma of the Prostate Gland, Arch. Surg. **43**: 209-223 (Aug.) 1941.

our clinic); (2) in that small percentage of patients in whom the diagnosis is in doubt, and (3) in certain feeble men until the condition of the patient improves.

It has been demonstrated [30] that the prostatic cancers may be grouped into two functional classes, androgen-dependent and androgen-independent, and the failures of treatment and the relapses after remission mostly fall in this latter group. Some of the failures after orchiectomy result, however, from the production of androgen in the adrenal glands,[31] and it is our custom to administer estrogen to those patients who have evidence of a relapse or failure after orchiectomy.

(*c*) Irradiation: External irradiation has never been spectacularly successful in the treatment of prostatic cancer; it is capable of producing palliation and relief of pain in certain cases of osseous metastasis, and it is used in our clinic in the treatment of appropriate patients in relapse.

Clinical Notes, Suggestions and New Instruments

BAL THERAPY OF THROMBOPENIC PURPURA AFTER ARSPHENAMINE TREATMENT

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Porsgrunn, Norway

While prognosis is generally more favorable in cases of idiopathic thrombopenia, life is often endangered if thrombopenia develops during treatment of syphilis with arsenic compounds.

Guided by a report by Lockie, Norcross and George [1] of a case in which thrombopenia and granulocytopenia occurred after treatment with colloidal gold, with recovery after BAL (2,3 dimercaptopropanol) therapy, I administered BAL in a case of thrombopenic purpura after neoarsphenamine intoxication. The response was favorable.[1]

REPORT OF CASE

A woman aged 34, who weighed 63 Kg., was delivered to our service on June 27, 1947 complaining of bleeding from her gums, multiple hemorrhages into the skin and metrorrhagia. These symptoms were manifest from early in the morning the same day she entered our service. Her syphilis had been diagnosed in October 1946 and she had been under antisyphilitic treatment since then; she had received a total amount of 10 Gm. of neoarsphenamine. She complained of general malaise some weeks before being hospitalized.

Examination of her blood gave the following results: prolonged bleeding time (twenty minutes); normal coagulation time (two minutes), and 7,500 thrombocytes per cubic millimeter. In the bone marrow there occurred an increased number of megakaryocytes, chiefly young forms.

Treatment with BAL started on June 28 but was stopped again on June 29. The amount of BAL was 13.5 cc. Her condition improved considerably during the first twenty-four hours afterward and bleeding from her uterus had stopped almost completely. Furthermore, all bleeding, including metrorrhagia, had completely stopped after forty-eight hours, on June 30.

Treatment with BAL was stopped to exclude the possibility of a post hoc and not propter hoc effect. Her condition remained excellent until July 8, when she complained of bleeding from the gums again; on July 9 she complained of profuse metrorrhagia. Treatment with BAL was recommended with 1.8 cc. of a 10 per cent solution every four hours for forty-eight hours and thereafter 1.6 cc. at the same intervals for forty-eight hours and 1.5 cc. two times daily until the tenth day. All bleeding had stopped on July 12, after seventy-two hours of treatment. After BAL therapy the platelet count rose again from 2,500 to 280,000.

Representative Hematologic Data

Date, 1947	Hemoglobin, Percentage	White Blood Cell Count	Platelets	Comment
6/27.....	105	5,800	7,500	
6/28.....	105	.....	7,500	BAL therapy, 13.5 cc.
6/29.....	..	.....	7,500	BAL therapy stopped
6/30.....	..	.....	10,000	
7/ 1.....	..	.....	12,500	
7/ 3.....	..	.....	71,250	
7/ 5.....	..	.....	82,500	
7/ 7.....	..	.....	22,500	BAL therapy recommenced
7/ 9.....	85	.....	2,500	
7/10.....	..	.....	6,250	
7/11.....	..	.....	26,250	
7/12.....	67	5,650	36,750	
7/14.....	..	6,200	168,750	
7/15.....	..	6,150	193,750	
7/16.....	..	6,000	243,500	
7/18.....	..	5,450	280,000	BAL therapy stopped
7/21.....	73	5,200	217,500	
7/24.....	86	5,175	113,000	
7/26.....	80	4,700	97,500	

Representative hematologic data are given in the table.

SUMMARY

A case is described of serious thrombopenia after antisyphilitic arsenotherapy in which treatment with BAL was successful.

30. Huggins, C.: Prostatic Cancer Treated by Orchiectomy: The Five Year Results, J. A. M. A. **131**: 576-581 (June 15) 1946.

31. Huggins, C., and Scott, W. W.: Bilateral Adrenalectomy in Prostatic Cancer: Clinical Features and Urinary Excretion of Seventeen-Ketosteroids and Estrogen, Ann. Surg. **122**: 1031-1041 (Dec.) 1945.

From the medical department of St. Joseph's Hospital; chief, Dr. A. Schrumpf.

Dr. Harry Eagle of the Johns Hopkins Hospital and the United States Public Health Service furnished the supply of BAL, which is not yet available in Norway.

1. Lockie, L. M.; Norcross, B. M., and George, C. W.: The Treatment of Two Gold Reactions (Thrombocytopenia and Granulocytopenia) with BAL, J. A. M. A. **133**: 755 (March 15) 1947.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

AUSTIN SMITH, M.D., *Secretary.*

INFLUENZA VIRUS VACCINE, TYPES A AND B.—A sterile formaldehyde-killed suspension in isotonic sodium chloride solution of influenza virus consisting of 50 per cent type A virus (equal parts of PR[8] and Weiss strains) and 50 per cent type B virus (Lee strain) obtained by separate propagation in the extraembryonic fluids of the developing chick and refined and concentrated either by the red cell elution method or by the centrifugation method. The chosen strains are antigenically distinct and are representative of two known etiologic types of influenza virus, cross immunization with which does not occur. The vaccine is standardized for immunizing potency, purity and sterility in accordance with recommendations of the National Institute of Health.

Actions and Uses.—Influenza virus vaccine is used for the production of active immunity against influenza, especially when an epidemic is threatened. Its prophylactic value has been observed only for mild types of influenza and is not fully established against severe outbreaks of the disease. Immunity is conferred whose duration ranges from about three months to one year, so that it is advisable to repeat immunization at least every six months when there is need for continued protection. Evidence thus far available indicates that the vaccine is principally effective in reducing the incidence of type B infections; its ultimate protective value in type A influenza is under observation. Its use is recommended against only those strains from which it is prepared and does not render protection against influenza due to other strains of the virus.

In persons allergic to chick or egg protein or who have been sensitized by previous administration of vaccines prepared from

chick embryos the use of the vaccine may be potentially dangerous. A careful history to rule out allergy to egg protein should be taken, and, if necessary, an intracutaneous test dose should be given to determine the presence or absence of sensitivity. Patients definitely allergic to chick or egg protein should not be immunized.

Dosage.—A single immunizing dose of 1 cc. administered subcutaneously is usually sufficient to induce active immunity within one to two weeks. For children under 12 years of age the dose should not exceed 0.5 cc., with proportionately less for the very young because of greater toxicity of the vaccine in children. A second injection may be indicated if outbreaks of influenza appear in severe form.

PITMAN-MOORE COMPANY, DIVISION OF ALLIED LABORATORIES, INC., INDIANAPOLIS

Influenza Virus Vaccine, Types A and B, Refined and Concentrated: Packages of one vial, 5 cc. (five doses). Preserved with sodium ethyl mercuri thiosalicylate 1: 10,000.

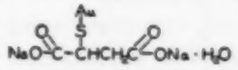
SHARP & DOHME, INC., GLENOLDEN, PA.

Influenza Virus Vaccine, Types A and B, Protamine Concentrated and Refined: Packages of twenty-five, 1 cc. vials. Preserved with sodium ethyl mercuri thiosalicylate 1: 10,000.

E. R. SQUIBB & SONS, NEW YORK

Influenza Virus Vaccine, Types A and B, Refined and Concentrated: Packages of 1 cc. and 10 cc. vials. Preserved with sodium ethyl mercuri thiosalicylate 1: 10,000.

GOLD SODIUM THIOMALATE.—Myochrysine-Merck. —*Di*sodium aurothiomalate. — $C_4H_2O_4SAuNa_2.H_2O$. — M. W. 408.33. A gold salt formed by the interaction of sodium thiomalate and a gold halide. It contains about 50 per cent of gold.



Actions and Uses.—Gold sodium thiomalate, like other gold salts, is indicated for the treatment of established cases of active rheumatoid arthritis and for the treatment of nondisseminated lupus erythematosus. Against rheumatoid arthritis it is most effective in relatively early cases, before development of extensive deformities. Gold sodium thiomalate is of no value in the treatment of other arthritides. See also the statement on Gold Compounds (N. N. R. p. 477).

Dosage.—For active rheumatoid arthritis, an initial intramuscular dose of 10 to 15 mg. is suggested in all patients to test tolerance to the drug. Subsequent doses of 25 to 50 mg. at weekly intervals may be given for a total of 700 to 2,000 mg. as a single course. A total amount not to exceed 500 to 1,000 mg. is considered safer. A minimum of two courses is generally given, with an intervening rest period of six to twelve weeks.

For localized lupus erythematosus an initial dose of 5 mg., increased by that amount at weekly intervals to a maximum of 50 mg. for women or 75 mg. for men, is usually recommended.

Toxic reactions are generally minimized by the use of weekly doses not to exceed 25 mg. Transient flushing of the face with giddiness and vertigo may be observed following administration.

Tests and Standards.—

Gold sodium thiomalate occurs as a fine, white to yellowish white powder possessing a metallic taste. It is extremely soluble in water; practically insoluble in alcohol and in ether. Aqueous solutions of gold sodium thiomalate are colorless to pale yellow. The *p*H of a 5 per cent aqueous solution is between 5.8 and 6.8.

Dissolve about 50 mg. of gold sodium thiomalate in 5 cc. of water and divide the solution into four portions. To one portion add about 0.25 cc. of calcium nitrate solution; a white precipitate is formed, which dissolves on addition of diluted nitric acid but reprecipitates on the addition of ammonium acetate solution. To a second portion add 1 cc. of calcium nitrate solution, mix and centrifuge. Decant the supernatant liquid and add 0.25 cc. silver nitrate solution: no precipitate results. To a third portion add about 0.25 cc. of silver nitrate solution: a yellowish precipitate is formed, which dissolves completely on the addition of an excess of ammonium hydroxide solution. To the fourth portion in a porcelain dish add about 0.25 cc. of ammonium hydroxide solution and 0.25 cc. of 30 per cent hydrogen peroxide, evaporate and ignite. Add 5 cc. of water to the residue and filter the mixture: particles of gold are found on the filter, and the filtrate responds to tests for sodium and sulfate.

Dry about 0.5 Gm. of gold sodium thiomalate, accurately weighed, at room temperature in a desiccator over fresh phosphorus pentoxide for twenty-four hours: the loss in weight does not exceed 6.0 per cent.

Weigh, accurately, about 0.5 Gm. of gold sodium thiomalate and transfer it to a 300 cc. Kjeldahl flask with about 10 cc. of water; add 20 cc. of nitric acid and mix well. Add 15 cc. of sulfuric acid slowly with mixing and heat over a low flame, at first gently boiling and later increasing the heat until fumes of sulfur trioxide are evolved. Allow the flask and contents to cool to room temperature and add 30 cc. of water slowly with mixing. The precipitated gold should agglomerate, and the liquid should not have a purplish color (colloidal gold). If the liquid is not colorless, add 20 cc. of 3 per cent hydrogen peroxide, reheat as directed, recool and redilute. Filter through an ignited tared Gooch crucible, wash with water, dry at 100 C., ignite, cool and weigh: the weight of gold found corresponds to not less than 49.5 per cent and not more than 50.7 per cent, calculated to the dried substance.

MERCK & CO., INC., RAHWAY, N. J.

Solution Myochrysine: 1 cc. ampuls containing 10 mg., 25 mg., 50 mg. or 100 mg. of gold sodium thiomalate, equivalent to 5 mg., 12.5 mg., 25 mg. and 50 mg. of gold, respectively.

U. S. patent 1,994,213 (March 12, 1935; expires 1952) and U. S. trademark 318,890, both assigned to Société des usines Chimiques Rhône-Poulenc, Paris, France.

PICROTOXIN-U. S. P.—"An active principle obtained from the seed of *Anamirta Cocculus* (Linné) Wight et Arnott (Fam. *Menispermaceae*)." *U. S. P.*

For description and standards see the U. S. Pharmacopeia under Picrotoxin and Picrotoxin Injection.

Actions and Uses.—Picrotoxin is a stimulant and convulsant acting chiefly on the higher centers. Thus if the midbrain and pons are removed in mammals, the convulsive action disappears, although signs of medullary stimulation may persist. Aside from the convulsions which picrotoxin produces, the principal important actions are those relating to medullary stimulation. Acceleration of the respiratory rate, rise in blood pressure, slow pulse and nausea and vomiting are the usual effects observed after the administration of picrotoxin.

The principal use of picrotoxin is in the treatment of barbiturate poisoning. The drug has a special analeptic action against the narcosis induced by overdosage of the barbiturates; it will overcome the depression of respiration and increase the oxygen consumption of the poisoned animal. The period of narcosis is appreciably shortened. Although highly poisonous to normal persons, the toxicity of picrotoxin appears to be less in persons narcotized by the barbiturates. The drug is rapidly destroyed in the body.

Dosage.—In cases of barbiturate poisoning, 1 to 3 mg. should be administered intravenously or 3 to 6 mg. intramuscularly every fifteen minutes until the desired response is obtained. Artificial respiration, an open airway, oxygen, gastric lavage and intravenous fluids should be employed concurrently with the picrotoxin therapy.

ABBOTT LABORATORIES, NORTH CHICAGO, ILL.

Picrotoxin Solution, 0.3 Per Cent: 20 cc. vials. Each cubic centimeter contains picrotoxin 3 mg. and benzyl alcohol 1.5 per cent, in isotonic sodium chloride solution.

PENICILLIN (See New and Nonofficial Remedies, 1947, p. 144).

The following additional dosage forms have been accepted:

COMMERCIAL SOLVENTS CORPORATION, TERRE HAUT, IND.

Crystalline Penicillin G Potassium in Oil and Wax: 300,000 units in 1 cc. One 1 cc. glass cartridge in package with disposable plastic syringe and needle assembly; five 1 cc. glass cartridges in package with or without permanent syringe assembly consisting of metal syringe and two stainless steel 1½ inch (3.8 cm.) 20 gage needles. Potassium penicillin G suspended in peanut oil containing 4.8 per cent white wax U. S. P.

PREMO PHARMACEUTICAL LABORATORIES, INC., NEW YORK

Crystalline Penicillin G Sodium: 20 cc. vials containing 500,000 units and 1,000,000 units.

Penicillin Calcium Ointment: 28.5 Gm. tubes. Each gram contains 2,000 or 5,000 units of penicillin calcium in a base consisting of white petrolatum U. S. P. and anhydrous wool fat.

Crystalline Penicillin G Sodium in Oil and Wax: 300,000 units per cubic centimeter in 1 cc. glass hypodermic syringe. Crystalline penicillin G sodium suspended in sesame oil containing 4.8 per cent white wax U. S. P.

CHORIONIC GONADOTROPIN (See New and Nonofficial Remedies, 1947, p. 374).

The following dosage forms have been accepted:

GEORGE A. BREON & COMPANY, INC., KANSAS CITY, MO.

Chorionic Gonadotropin, 10,000 International Units: 10 cc. vials. A powdered preparation of chorionic gonadotropin packaged in vials which, when treated with the accompanying 10 cc. ampul of phosphate buffer solution, furnishes a solution containing 1,000 international units.

COLE CHEMICAL CO., ST. LOUIS 8

Chorionic Gonadotropin, 1,000 and 5,000 International Units: 10 cc. vials. Powdered preparations of chorionic gonadotropin which, when diluted with the accompanying 10 cc. vial of sterile distilled water containing 0.2 per cent metacresol, provide solutions having a potency of 100 and 500 international units per cubic centimeter, respectively.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, DECEMBER 27, 1947

HYGIENE OF THE VOICE

Man is the talking animal, communicating by the use of speech. When a man loses his voice, he is said to be dumb; peculiarly the word also has the meaning of stupid. Perhaps the reproach is unwarranted, because medical science has certainly given far too little consideration to a faculty as important as is speech. Occasionally specialists in otolaryngology make scientific studies of the movements of the vocal cords and of such gross conditions as tuberculosis and cancer which may affect them. Still undecided, however, are the multiple causations of stuttering or stammering. The immense importance attached to radio and public speaking in our modern civilization has brought into the field a number of teachers of voice placement. Persons who formerly were unable to hold audiences because of the high pitch or shrill character of their voices learn to speak with a low pitch. A defect of speech is a mental, social and economic handicap, resulting in embarrassments and disturbances in family, industrial and political life. Many scientists are convinced that the factors involved in speech difficulties are primarily mental or emotional.

Functional impediments to speech, such as chronic hoarseness and phonasthenia, Froeschels [1] believes are the result of phobias due to hyperfunction or hypofunction of the vocal apparatus. The hyperfunction produces the impression of strain; the hypofunction, an impression of flabbiness. Among the psychogenic troubles of the voice, spastic and paretic aphonias are included. Analysis of the voice of nursing infants shows that they have two different cries; one has a soft beginning and the other a hard beginning. The soft onset is significant of a good mood, but the hard one indicates distress.

Froeschels found that 93 per cent of the preschool children in Vienna had hoarse voices. He examined the voices of 1,000 school children while they were speaking and while they were reading. The few who did not show straining of the voice during speaking showed it during reading. The slight emotion produced by the difficulties which reading offers a child seems to be one of the reasons for the sudden increase in hyperfunction. Contrasting with hyperfunction of the muscles of the glottis and those of the upper resonating cavities is hypofunction, to which Jackson gave the name myasthenia of the larynx. The paretic or hypofunctional state may be characterized by relaxation of the muscles which close the glottis and probably of some pharyngeal muscles also.

Froeschels describes an original method of treating functional disturbances of voice which he designates as the chewing method. The idea is based on the observation that one can chew, speak and even sing at the same time. Since the same muscles and the same nerves of the upper resonating cavities are engaged in the two functions, he concludes that chewing and speaking must be somewhat identical. The argument is that one cannot perform two different actions at the same time with one set of muscles. Long observation convinced Froeschels that chewing was the origin of human speech. It appears that members of primitive tribes continually produced voice during chewing. Mammals frequently produce voice while chewing. He sees further proof in the fact that a deaf mute will suddenly acquire a pleasant voice when ordered to chew with voice production. The method, Froeschels reports, has been tried on thousands of patients.

The patient is asked to chew as usual with closed lips, but without anything in the mouth, and to observe his tongue, which moves continually during the chewing. Immediately afterward he is asked to chew "like a savage," that is, by opening the mouth and with extensive movements of the lips and tongue. Many people when chewing with open mouth have the tongue continually on the floor of the mouth but that, according to Froeschels, is not the way savages chew, who lift and drop the tip of the tongue. Only the original method of chewing guarantees the setting free of the voice. Then the patient must give voice during chewing. If the chewing is done correctly, that is with vigorous movements of the lips and tongue, a great variety of sounds escape the mouth. As a result of these chewing exercises, the hyperfunctional voice changes immediately into a free and normal one. Abnormally low female voices rise during chewing.

The patient is advised to chew with voice production at least twenty times a day for a few seconds only but should always avoid doing so mechanically. He should act with the guiding idea of having some food in his mouth. After a few days he should read several times a day for one or two minutes only but should begin with a voiced "nonsense" chewing and should always, after having read some words, introduce another "nonsense" chewing. Froeschels claims success in the treatment of severe hyperfunctional and hypofunctional states of the voice as well as in less severe cases, such as the severe breaks of the voice

1. Froeschels, E.: Hygiene of the Voice, Arch. Otolaryng. **38**: 122 (Aug.) 1943.

during the change at puberty, and in the management of the pathologic sequelae of change of the voice, such as the eunuchoid and the perverse voice change.

In his well known textbook on "Diseases of the Nose, Throat and Ear," Dr. Chevalier Jackson [2] notes that one of the pitfalls in the treatment of laryngeal weakness is the belief that some different system of vocal training or some special exercises will cure the overworked muscles. He feels that absolute rest is necessary before any new system of training is undertaken so that the muscles may recover from the damage previously done. His regimen includes a period of absolute silence at least half as long as the duration of the strenuous use of the voice; next, omission of any use of the voice on days when there is especially strenuous vocal work; he recommends absolute silence on the weekend and elimination of all attempts to talk against noise. Any necessary use of the telephone is to be done with a low voice and with the telephone transmitter held close to the lips. Especially dangerous is an attempt by singers or public speakers to extend the range of pitch upward.

Certainly more study is needed on both the hygiene of the voice and the technics desirable to strengthen and prolong its function.

GLUTAMIC ACID

In several articles recently published in popular periodicals experimentation with glutamic acid has been strongly exploited, emphasizing its effects in raising general intelligence levels in subnormal patients. The general public is being well informed of advances in experimental medicine, but some of the side effects concerning which THE JOURNAL has warned repeatedly are less desirable. Even vast amounts of glutamic acid will not enable morons to approach genius overnight.

Pressure of "patient opinion" may force physicians to prescribe products still in an early experimental stage. In recent years latent kidney damage appeared from the use of sulfonamide compounds, dermatitis and allergic reaction from antibiotics, unfavorable reactions from racemic amphetamine sulfate ("benzedrine sulfate") prescribed too frequently or in excessive amounts and toxic reactions from the antihistamine drugs.

Experimental work thus far reported includes study of effects of the administration of glutamic acid on intelligence of white rats and human beings. The latter studies were made mostly on children and adolescents of subnormal mental status or those with a history of convulsive attacks (Zimmerman and Ross,[1] Price, Waelsch and Putnam,[2] and Zimmerman, Burgemeister and Putnam [3]). White rats were made to perform intricate maze problems in order to obtain food; the group fed glutamic acid revealed a greatly increased ability to solve the maze problems. Effects were essentially the same with both *l*-glutamic acid (naturally occurring) and *dl*-pyrrolidine carboxylic acid. Growth curves for rats fed glutamic acid remained the same as those for controls, so it was believed that inanition did not play a part in the results obtained. In vitro an increased rate of production of acetylcholine occurs in the presence of glutamic acid. Results were believed to be related to a parallel increase of acetylcholine in the rats fed glutamic acid.

In human subjects the administration of *dl*-glutamic acid was tried in conjunction with other known anticonvulsant therapy with groups of patients having grand mal, petit mal and psychomotor discharge types of attacks.[2] Psychomotor and petit mal attacks were definitely decreased in frequency, and increased mental and physical alertness of patients was observed. Grand mal seizures were unaffected. In all cases tolerance to *dl*-glutamic acid hydrochloride was high. Gastrointestinal reaction was minimal and other untoward symptoms absent.

Effects of the drug in 69 children and adolescents were studied [3]: 28 patients, 11 mentally retarded, had a history of convulsive disorders; 33 were mentally retarded only. Glutamic acid was fed in gradually increasing doses. The average dose was 12 Gm. per day, with a 6 to 24 Gm. range. Several intelligence tests including intelligence quotients and Rorschach tests were given initially and during treatment. Differences were measured. The most striking changes occurred with the mentally retarded group, in which statistically significant changes were observed. These and other experiments showed average increases in intelligence quotients from 8 to 11 points while taking glutamic acid. Indications are that the gain is not permanent. Petit mal seizures and psychomotor disturbances alleviated with glutamic acid apparently tended to return when administration of the agent was stopped. The results thus far reported with glutamic acid in the types of cases mentioned are considered excellent. However, experiments are still under way.

The truly miraculous progress of medicine in recent years has stimulated a public attitude of expectancy that many medical problems now unsolved will soon be fathomed. Inevitably disappointment will result in several instances. Most advances result from progressive accretion of knowledge over a number of years. Occasionally what appears to be definite progress turns out to be merely insufficient and uncontrolled experimentation.

2. Jackson, C., and Jackson, C. L.: Diseases of the Nose, Throat, and Ear, Including Bronchoscopy and Esophagoscopy, Philadelphia, W. B. Saunders Company, 1945.

1. Zimmerman, F. T., and Ross, S.: Effect of Glutamic Acid and Other Amino Acids on Maze Learning in the White Rat, Arch. Neurol. & Psychiat. **51**: 446 (May) 1944.

2. Price, J. C.; Waelsch, H., and Putnam, T. J.: dl-Glutamic Acid Hydrochloride in Treatment of Petit Mal and Psychomotor Seizures, J. A. M. A. **122**: 1153 (Aug. 21) 1943.

3. Zimmerman, F. T.; Burgemeister, Bessie B., and Putnam, T. J.: Group Study of Effect of Glutamic Acid on Mental Functioning in Children and Adolescents, Psychosom. Med. **9**: 175 (May-June) 1947.

Current Comment

LEPROSY APPARENTLY CONTRACTED BY INOCULATION

Whether or not leprosy can be contracted by inoculation has been debatable. Profeta [1] inoculated 10 persons experimentally without reproducing the disease. Danielssen [2] repeatedly inoculated himself but did not show evidence of leprosy. Marchoux,[3] while operating on a leper, pricked the finger of his assistant, in whom leprosy developed after several years. In Lagoudaky,[4] who was repeatedly injected with blood from a leper, there developed cutaneous lesions of leprosy less than two months after his first inoculation. These and other references are cited by Porritt and Olsen,[5] who report the cases of 2 United States Marines who were tattooed by the same man on the same day at Melbourne, Australia, in June 1943. Both marines contracted leprosy in the tattoos during the first half of 1946. One man had multiple tattoos on his left arm, but leprosy developed only in the one made in Melbourne on the day when his friend was tattooed and a number of needles were broken during the tattooing. Biopsies were made in the 2 cases, and unstained sections were submitted to the U. S. Public Health Service. From the Marine Hospital (leprosarium) at Carville, La., came the following diagnosis: typical tuberculoid leprosy. These cases provide strong evidence for inoculation as a method of transmitting leprosy.

BLEEDING IN THROMBOCYTOPENIC PURPURA

Allen and Jacobson,[1] who discovered the presence of an anticoagulant in hemorrhage produced in dogs experimentally by radiation, report that the tendency to bleed could be prevented or stopped temporarily by the intravenous injection of protamine sulfate or toluidine blue. Both these substances are apparently capable of binding heparin and rendering it biologically inactive. Allen and his associates [2] now report their clinical experience with administration of toluidine blue as a means of aiding in the control of petechial hemorrhages in thrombocytopenia. Four patients had thrombocytopenic purpura associated with acute or subacute leukemia; 2 had idiopathic thrombocytopenic purpuras. The dye was dissolved in 250 to 500 cc. of isotonic sodium chloride solution and administered in a dose of 1 to 4 mg. per kilogram of body weight. This was given intravenously over a two hour period. The administration of the dye had a dramatic effect on the petechiae. The authors emphasize that the bleeding usually will not entirely cease unless the platelet count is partially elevated by blood transfusions. When such bleeding persists after the appropriate administration of toluidine blue, transfusions of fresh whole blood should be given. Little is known of the toxicity of the dye, except that it is excreted in the urine and into the intestinal tract and is not active when given orally. The dye appears to affect capillary permeability, aiding only in controlling petechiae. The bleeding time is not shortened and bleeding from ulcerated or denuded areas is not materially altered unless whole blood transfusions are given or spontaneous platelet elevation occurs. The authors believe that these observations are probably of greater physiologic interest than therapeutic value in diseases characterized by a tendency to bleed.

1. Profeta, G.: Sulla elefantiasi dei Greci, Gior. internaz. d. sc. med. **6**: 282-299, 1884.
2. Danielssen, D. C., and Boeck, W.: Traité de la spédalskhed ou éléphantiasis des grecs, Paris, J. B. Baillière, 1848.
3. Marchoux, E.: Un cas d'inoculation accidentelle due bacille de Hansen en pays non lepreux, Internat. J. Leprosy **2**: 1-6, 1934.
4. Lagoudaky, S.: Preliminary Note on Self Inoculation of Leprosy, J. Trop. Med. **39**: 81-83, 1936; Self-Inoculation of Leprosy: Second Communication, ibid. **40**: 77-79, 1937.
5. Porritt, R. J., and Olsen, R. E.: Two Simultaneous Cases of Leprosy Developing in Tattoos, Am. J. Path. **23**: 805-811, 1947.
1. Allen, J. G., and Jacobson, L. O.: Hyperheparinemia: Cause of the Hemorrhagic Syndrome Associated with Total Body Exposure to Ionizing Radiation, Science **105**: 388, 1947.
2. Allen, J. G.; Bogardus, G.; Jacobson, L. O., and Spurr, C. L.: Some Observations on Bleeding Tendency in Thrombocytopenic Purpura, Ann. Int. Med. **27**: 382 (Sept.) 1947.

CENTER FOR STUDY OF INFLUENZA VIRUS STRAINS ESTABLISHED

The Commission on Influenza, Army Epidemiological Board, Office of the Surgeon General, U. S. Army, recognizing the potential importance in the epidemiology of influenza of antigenic differences among strains of influenza virus, has for several years maintained a center for the study of strains of influenza virus under the supervision of Dr. Thomas P. Magill at the Cornell University Medical College, 1300 York Avenue, New York. Because the problem is one of importance in the recurrence of epidemics and in the preparation of vaccines, the objectives of the Influenza Virus Strain Study Center include a search for strains of broad immunizing potency and also a search for strains which differ sharply from the ones currently included in influenza virus vaccines. The center distributes potent antiserums in limited quantities for diagnostic purposes to U. S. Army laboratories and Influenza Commission field units; it serves also as a store for the preservation of strains of virus. Whether a large number of stable strains of influenza virus exist or whether the influenza virus is a relatively unstable agent, whose antigenic characteristics may readily change, has not been established. However, the rather sudden manner in which strains have appeared which differ sharply in antigenic characteristics from standard strains suggests that the latter alternative may be the correct one. Regardless of which alternative is correct, the fact that such strains do appear suddenly makes it imperative that a vaccination program include a careful watch for the appearance of significant variants. Obviously, the more widespread the watch, the greater the chances of success. The Commission on Influenza is endeavoring to broaden the watch for significant variants by increasing the interest in the accurate laboratory diagnosis of influenza. The Influenza Virus Strain Study Center offers a diagnostic service by which laboratories not equipped for the work may obtain rapid identification and serologic classification of strains which they have isolated. Even those laboratories which are prepared to identify the broad groups of the strains of the viruses of influenza A and influenza B are asked to submit such strains to the center for further study as soon as possible after isolation. Complete cooperation will aid the swifter advance of knowledge in this difficult field.

ORGANIZATION SECTION

Washington Letter

(From a Special Correspondent)

Dec. 18, 1947.

Increased Research in Pure Science

In his annual report of the Carnegie Institution, Dr. Vannevar Bush, president, reported increased research in pure science during the past year. The period was noteworthy for reorientation of research programs in light of wartime discoveries. Among various developments reported was the discovery that the same chemical agents which are known to produce cancer are now believed to be producers of mutations in germ cells of insects, resulting in different hereditary properties. The studies on cancer were conducted by the department of genetics and are considered to be an approach to determining the basic cause of malignant growths. Dr. Milislav Demerec, director, says that if the mutations theory is true, chances of early discovery of ways to prevent cancer are "very, very slight."

National Health Needs Reviewed

In a review of national health needs the Congressional quarterly points out the great variations between states and areas in facilities and personnel for dealing with health needs. The national shortage of hospital beds is cited; it is reported that in general only the principal cities have the desired ratio of 4.5 beds per thousand population. The 1942 national ratio of 3.5 beds per thousand persons is quoted, and it is stated that the situation has not improved much since. Nevada is shown with 7 beds per thousand, and Mississippi is given as having 1.6. Uneven distribution of physicians is noted, with the country in 1940 having one hundred and thirty-three for every hundred thousand persons, or about one for every seven hundred and fifty persons.

Atomic Commission Reports Discovery of New Isotope Tracers

The Atomic Energy Commission announced that various newly produced tracer materials for use in medical and other research where radioactive tracers are too dangerous have been developed. They are called "stable isotopes," in contrast with radioactive materials. Previously only five such stable isotopes were available, but one hundred additional stable isotopes are now being produced on a limited basis. A plan has been worked out for their distribution on loan to government research laboratories.

Construction of Veterans' Hospital

The Arlington County, Va., Board has reversed its former opposition to use of the Nevius Tract, adjacent to Arlington National Cemetery, as the site of a Veterans Administration hospital. Rep. Howard Smith, Democrat of Virginia, has agreed to back use of the land for this purpose in Congress, although he had previously blocked the proposal at the request of the county.

Dedicate Children's Wing of Hospital

A plaque bearing the likeness of the late President Roosevelt was unveiled by President Truman in the children's wing of the new Georgetown Hospital, financed by a $55,000 gift presented to Georgetown University by president Philip Murray of the Congress of Industrial Organizations on behalf of the union. Mr. Truman recalled the late president's interest in the health and welfare of children at Warm Springs Foundation for Infantile Paralysis. Very Reverend Lawrence C. Gorman, president of the university, said that the gift of the C. I. O. was the largest contribution toward construction of the new four hundred and seven bed hospital.

Veterans Administration Tightens Up Qualifications for Medical and Dental Treatment

The Veterans Administration announced that beginning January 1 ailments must be proved to be caused by military service before veterans can be admitted to veterans hospitals, authorized for outpatient care or given free dental treatment. Treatment is now given on the word of the veteran that ailments arose from military service, but after the first of the year military records must substantiate the source of injuries or illnesses before treatment is given. Officials claim that two thirds of all beds in Veterans Administration hospitals are occupied by veterans under treatment for ailments not connected with their service. Only 36,000 of 103,000 hospital patients are said to have service-connected medical ills.

Medical Aid for Navajo and Hopi Indians

The House Public Lands Committee approved a bill authorizing expenditure of $2,000,000 for emergency aid for Navajo and Hopi Indians in Arizona, New Mexico and Utah. Another bill will be required to provide funds. Expansion of medical facilities on Navajo and Hopi reservations is included in the aid program, along with direct relief for needy children and blind, disabled and aged Indians and building programs to provide jobs for the able bodied. At least 4,000 of the 64,000 members of the two tribes now need help, and the number may rise to 10,000 during the winter.

Hospital for Institute of Health

Federal planners reported that a combined five hundred bed hospital and medical research center is planned for early enlargement of the National Institute of Health at Bethesda, Md. Commissioner W. E. Reynolds of the Public Buildings Administration disclosed that Congress has allocated funds for plans and that the development will be built on property across Rockville Pike from the new naval hospital.

Coming Medical Meetings

American Medical Association Interim Session, Cleveland, Jan. 5-8. Dr. George F. Lull, 535 N. Dearborn St., Chicago 10, Secretary.

Annual Congress on Industrial Health, Cleveland, Jan. 5-6. Dr. Carl M. Peterson, 535 N. Dearborn St., Chicago 10, Secretary.

Annual Congress on Medical Education and Licensure, Chicago, Palmer House, Feb. 9-10. Dr. Donald G. Anderson, 535 North Dearborn St., Chicago 10, Secretary.

National Conference on Rural Health, Chicago, Palmer House, Feb. 6-7. Dr. F. S. Crockett, 535 N. Dearborn St., Chicago 10, Chairman.

American Academy of Orthopaedic Surgeons, Chicago, Palmer House, Jan. 24-29. Dr. Harold B. Boyd, 869 Madison Ave., Memphis, Tenn., Secretary.

American Society for Surgery of the Hand, Chicago, Jan. 23-24. Dr. Joseph H. Boyes, 1401 S. Hope St., Los Angeles 15, Secretary.

Southeastern Allergy Association, Richmond, Va., Jefferson Hotel, Jan. 17-18. Dr. Katharine B. MacInnis, 1515 Bull St., Columbia 49, S. C., Secretary.

GOVERNMENT SERVICES

VETERANS ADMINISTRATION

VETERANS ON DISABILITY COMPENSATION ROLLS

Nearly half of the 1,728,516 veterans of World War II on disability compensation rolls on June 30 had handicaps rated at 10 per cent, the minimum degree of impairment for which compensations are paid; only 1 in 20 veterans was totally disabled with a 100 per cent rating. Veterans with 20 per cent disabilities accounted for 12.7 per cent of the total; 30 per cent disabilities, 17.8 per cent; 40 per cent disabilities, 6.2 per cent, and 50 per cent disabilities, 9.4 per cent. Only 5.3 per cent of veterans drawing compensation payments had handicaps rated between 60 and 90 per cent.

Of the total cases on the rolls, about 1,228,000, or 71 per cent, were for disabilities resulting from general medical and surgical causes; 475,000, or 27.5 per cent, were neuropsychiatric cases, and the remaining 25,226, or 1.5 per cent, were cases of tuberculosis.

In the general medical and surgical category impairments of the joints, muscles and tendons were most prevalent, accounting for 485,467 cases. Communicable and infectious diseases were the causes for 144,637 compensation cases. Amputations accounted for only 25,065 cases, or 1.5 per cent of the general medical and surgical cases.

In the neuropsychiatric category, functional disorders of the nervous system were the reasons for 312,215 cases, or nearly two thirds of all the neuropsychiatric cases. Organic disorders of the nervous system accounted for 78,929 cases, and psychiatric disorders were the causes for 64,636 cases.

Veterans with diseases or injuries which were incurred in or aggravated by active military service, and which were not results of wilful misconduct, may obtain from the Veterans Administration monthly compensation payments ranging from $13.80 to $138 a month, according to the degree of disability. In certain severe disabilities such as blindness and the loss of limbs compensation payments may amount to as much as $360 a month.

SCHEDULE FOR BIDS ON SIXTEEN VETERANS' HOSPITALS

Sixteen contracts on Veterans Administration hospitals are expected to be awarded within the next sixty days. Recent revisions in hospital specifications eliminated the requirement for Saturday, Sunday and holiday work, and contractors are now able to figure with more certainty on labor costs. It has in effect established a forty hour week for this class of work and eliminated payments for overtime. According to the schedule set by the Army Corps of Engineers the closing dates for submission of general construction bids on nine hospitals will fall in December and early January. Contracts on acceptable bids will be made within thirty days following the opening date in each case. The hospitals, with the scheduled closing dates for general construction bids, are: Buffalo, 1,000 beds, December 4; Clarksburg, W. Va., 200 beds, December 29; Big Spring, Texas, 250 beds, January 5; Grand Island, Neb., 200 beds, December 15; Fort Wayne, Ind., 200 beds, December 19; Poplar Bluff, Mo., 200 beds, December 23; Iron Mountain, Mich., 200 beds, December 23; Omaha, 500 beds, January 5, and Beckley, W. Va., 200 beds, January 8.

In addition, invitations for bids on general construction work on seven hospitals will be advertised on the following schedule: Wilmington, Del., 300 beds, December 15; Altoona, Pa., 200 beds, December 10; Albany, N. Y., 1,000 beds, December 10; Little Rock, Ark., 500 beds, December 15; Wilkes-Barre, Pa., 475 beds, December 15; Erie, Pa., 200 beds, January 6, and Newark, N. J., 1,000 beds, early in 1948.

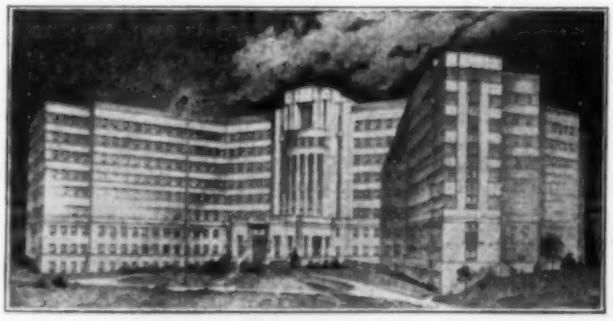
The closing date for bids on each hospital is about six weeks after advertisement of invitations to bid.

NEW TYPES OF ARTIFICIAL ARMS

The Veterans Administration announces that it is distributing three new types of artificial arms to some 5,000 amputee-veterans, through artificial limb dealers throughout the nation. The new artificial arms, which are the first concrete products of an artificial limb program financed by the government, are available to civilian amputees through the same distributors. These arms have improvements that enable amputees to operate them with greater ease and for more uses than was possible with the former artificial arms. Veterans who have permanent and spare arms of the older variety may secure one of the three new types as an additional or third arm most suitable to their needs provided the new appliance can be fitted satisfactorily. Amputee-veterans who have not yet received permanent and spare arms may select any appliance available, including the three new types, but they will be limited to a permanent and a spare arm, with hands or hooks for each. Information will be found in a booklet entitled "News About Artificial Arm Developments" at any Veterans Administration office.

HOSPITAL AT LOUISVILLE, KY.

The nine story, seven hundred and fifty bed hospital for the Veterans Administration in Louisville, Ky., will be erected on the 45 acre tract of land on Zorn Avenue which until recently was owned by the Louisville Water Company. The tract is on a bluff overlooking the Ohio River away from the thickly populated section. In addition to the hospital building, there will be a nurses' home, a two story residence for the manager, and two duplex two story buildings for resident physicians, a boiler house and a garage. The building will be equipped with automatic sprinklers. A hundred car parking lot and grounds for baseball, football, golf, tennis and basketball will be provided. Work on the main hospital building, which will occupy a full-sized block, will start early in the spring, according to Col. B. B. Talley, U. S. Army district engineer.



Veterans' hospital to be erected in Louisville, Ky.

MEDICAL BOOKS POPULAR AMONG VETERANS

Books in Veterans Administration technical medical libraries increased in number 14.5 per cent during a six month period ending October 1, according to F. R. St. John, director of the library service. Medical works in veterans' hospital libraries rose to 98,115. The total number of fiction and popular nonfiction volumes in hospital libraries for patients increased only 2.7 per cent during the same period. The reason for the rapid increase in medical volumes, St. John explained, was the emphasis placed on the acquisition of technical works during the latter part of the fiscal year. Circulation during September averaged 2.12 books per patient, compared with 1.99 per patient in June, 2.11 in July and 2.13 in August.

Medical News

(Physicians will confer a favor by sending for this department items of news of general interest: such as relate to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.)

CALIFORNIA

Society News.—At a recent meeting of the California Society of Internal Medicine Dr. Donald E. Griggs, Los Angeles, was elected president and Dr. DeWitt K. Burnham, San Francisco, secretary-treasurer.

Clams and Typhoid.—The California Department of Public Health states that 5 cases of typhoid were reported during October and that all of the patients were reported to have eaten raw clams in Pismo Beach, San Luis Obispo County. One death has occurred. Quarantine has been placed on clams and other shellfish in the area by the local health department, and the state health department is assisting the investigation.

Dr. Carpenter Heads Department of Infectious Diseases.—Dr. Charles M. Carpenter, Rochester, N. Y., has been appointed professor and chairman of the department of infectious diseases at the Medical School of the University of California, Los Angeles, effective January 1. This will be a major department which will include bacteriology, virology, parasitology and tropical medicine. Dr. Carpenter was formerly associate professor of bacteriology and public health at the University of Rochester School of Medicine and Dentistry, Rochester, N. Y. Dr. Ruth A. Boak, formerly associate in bacteriology at the University of Rochester School of Medicine and Dentistry, has been appointed associate professor of infectious diseases at the medical school, effective January 1.

COLORADO

Appointment in Pediatric Department.—Dr. John A. Lichty, Rochester, N. Y., has been appointed to the staff of the University of Colorado Medical Center, Denver, as assistant professor of pediatrics. Dr. Lichty will be in charge of the postgraduate pediatric educational program of the Colorado State Department of Health and the University of Colorado and will assist in developing the rural intern training program, the premature baby program, well baby conferences and the rheumatic fever program, which are joint responsibilities of the state health department and the university. Dr. Lichty graduated from the University of Rochester School of Medicine and Dentistry, Rochester, N. Y., in 1932 and served there as instructor and assistant professor of pediatrics. During the war he served with the Navy in the department of biologic warfare at Camp Detrick, Md.

CONNECTICUT

First Nutrition Institute.—The Connecticut State Department of Health, in cooperation with seven other agencies, sponsored its first Nutrition Institute recently in New Haven at the Yale University School of Nursing. Participating agencies included the Connecticut State Department of Education, Connecticut Home Economics Association, Connecticut Dairy and Food Council, Connecticut Dietetic Association, University of Connecticut, Storrs, American Red Cross, and Yale University. The annual meeting of the Connecticut Dietetic Association was held during the institute sessions.

Extend Consideration of Proposed Insurance Program.—The house of delegates of the state medical society voted at their recent semiannual meeting in New Haven to extend for sixty days consideration of a proposed program for the insurance of employed groups against the costs of surgery and maternity care. The action was taken to allow time for special meetings on the proposal by the society's eight component county associations. At the end of the sixty day period the house of delegates will be called into special session to act on the recommendations of the county associations, according to the vote. The plan would provide insurance against surgical and obstetric costs for family subscribers with incomes at or below $3,000 per year and for individuals with incomes at or below $2,000 per year. Individuals and heads of families with incomes above these levels would receive benefits commensurate with income, according to a schedule of indemnities. The proposed medical service would be offered to employed groups as a new type of insurance coverage through insurance carriers whose contracts are endorsed by the state medical society. Dr. James R. Miller, Hartford, president of the Connecticut State Medical Society and member of the Board of Trustees, American Medical Association, is chairman of the committee which prepared the plan.

GEORGIA

Dr. Abercrombie Honored.—Over three hundred employees of the state health department recently honored Dr. Thomas F. Abercrombie, Atlanta, at a reception on his thirtieth anniversary as director of the department. Acting Governor Thompson thanked Dr. Abercrombie on behalf of "more than three million Georgians who have benefited from the health program."

ILLINOIS

Services Offered to Physicians.—Information regarding the services now offered to Illinois physicians by the state department of public health is presented in circular 163, "Public Health Services for Illinois Physicians," available without charge from any local health department or from the Springfield offices. The circular contains instructions regarding the submission of specimens for laboratory tests and a directory of the state's laboratories, venereal disease treatment centers, cancer diagnostic clinics and all local health offices in Illinois.

Lectures Arranged by the State Society.—The Scientific Service Committee of the Illinois State Medical Society has arranged a lecture for the Will-Grundy County Medical Society January 22 in Joliet, where Dr. Israel Davidsohn, Chicago, will speak on "The Rh Factor." Lectures arranged through the education committee of the state society are:

January 9, Monmouth Women's Club, Dr. Raymond E. Davies, Spring Valley, What We Can Do About Cancer.
January 11, Young Married Couples' Sunday Evening Club, Chicago, Dr. Leon M. Hart, Chicago, Medicine in World War II.
January 17, Women's Club of Springfield, Dr. Harlan A. English, Danville, Compulsory Health Insurance.
January 20, Calumet High School Parent Teachers Association, Chicago, Dr. Ernst Schmidhofer, Chicago, Physical, Mental and Emotional Needs of Children.
January 23, Chicago Woman's Aid Club, Dr. John T. Reynolds, Chicago, Advances in Cancer.
January 23, Aux Plaines Branch, Chicago Medical Society in Oak Park, Dr. Harold W. Miller, Chicago, Prepayment Medical Care Plan.

Chicago

Cancer Clinic at Henrotin Hospital.—Henrotin Hospital will open a cancer prevention clinic for men with a complete male staff January 13 under the sponsorship of the Cancer Prevention Center of Chicago, Inc., which also operates a clinic for women at the Women's and Children's Hospital. Male physicians are to be added to the board and medical committee of the center. Some time in February the center will also open another clinic at Henrotin Hospital to take care of the women on the long waiting list at Women's and Children's Hospital, which has served women from throughout the United States and some foreign countries as well.

Establish Department of Clinical Science.—A department of clinical science has been established at the Chicago Professional Colleges of the University of Illinois to emphasize the interdependence of the basic sciences and the practice of clinical medicine. Dr. Andrew C. Ivy will head the new department. Research will be conducted on normal and pathologic gastrointestinal physiology, the biology of cancer, the vital function of the kidneys and the mechanisms and most effective means of producing analgesia. Four faculty members with the rank of assistant professor have been assigned to the department, and five research fellows and thirty graduate students also are conducting research. The department is offering three courses on "Advanced Physiology of the Digestive System," "Seminar in Clinical Science" and "Research in Clinical Science" for graduate students during the current semester. A fourth course, "Physiology of Symptoms," is offered to undergraduate medical students.

INDIANA

Society News.—Dr. Willis D. Gatch, Indianapolis, formerly dean of the Indiana University School of Medicine, Bloomington-Indianapolis, for fourteen years, was chosen president-elect of the Indianapolis Medical Society. Dr. Bert E. Ellis, Indianapolis, will be president of the society in 1948.——Dr. Roscoe L. Sensenich, South Bend, President-Elect of the American Medical Association, and Dr. Morris Fishbein, Editor of THE JOURNAL, addressed the December 2 meeting of the Elkhart County Medical Society, Elkhart, and later addressed a public meeting on the ten point program of the American Medical Association.

Hospitals to X-Ray All Patients Admitted.—On recommendation of the Vanderburgh County Medical Society, patients admitted to any of Evansville's three major hospitals will have roentgen examinations in search of tuberculosis. The program will begin early in 1948. It was proposed in a resolution adopted by the medical society in November and subsequently adopted by the Evansville Hospital Council. The three hospitals are buying special equipment, and expect to start the new program simultaneously. The plan also includes chest x-rays for all hospital executives and employees. The program is designed to prevent the spread of tuberculosis.

IOWA

Dr. Womack to Head Surgery Department.—Dr. Nathan A. Womack, associate professor of clinical surgery and surgeon to the outpatient clinics at Washington University School of Medicine, St. Louis, has been appointed professor of surgery and head of the department of surgery at the State University of Iowa College of Medicine, Iowa City, effective July 1. He succeeds Dr. Frank R. Peterson, who resigned in August, and will replace Dr. Robert T. Tidrick, associate professor, who has been acting head of the department. Dr. Womack, a graduate of Washington University School of Medicine, St. Louis, 1924, is a diplomate of the American Board of Surgery. He is also associate surgeon at Barnes General, St. Louis Children's and St. Louis Maternity hospitals.

MICHIGAN

Secretaries and Public Relations Conference.—The annual County Secretaries and Public Relations Conference of the Michigan State Medical Society will be held January 25 at the Book-Cadillac Hotel, Detroit. At the morning session Dr. Robert L. Novy, Detroit, president, Michigan Medical Service, will speak on "What the Voluntary Program Has Accomplished in the Distribution of Medical Service"; Dr. Wilfrid Haughey, Battle Creek, editor of the state journal, "Warning from Washington"; Edward F. Sladek, Traverse City, president-elect of the state society, "Making Friends for Medicine," and Dr. Roland M. Klemme, St. Louis, "Selling Health." The after dinner speaker will be Dr. Elmer Hess, Erie, Pa., president, Medical Society of the State of Pennsylvania, whose subject will be "The Physician Looks at the Future." Two panel discussions are scheduled for the afternoon beginning at 2:30: one on County Medical Society Organization, Dr. Otto O. Beck, Birmingham, Ala., as moderator; another on Mediums with Dr. Leroy W. Hull, Detroit, chairman of the state medical society's Public Relations Committee, as moderator. Guest speakers on the latter panel are Arthur L. Snider, Chicago, science editor, *Chicago Daily News*; William C. Hedges, New York, vice president, National Broadcasting Company, and Jam Handy, Detroit, president, Jam Handy Associates.

MISSOURI

Monthly Meetings for General Practitioners.—The American Academy of General Practice of Greater St. Louis is providing postgraduate training for the general practitioner by having monthly meetings in the St. Louis Medical Society Building. Well known speakers are guests of the organization. Their topics of discussion are limited to problems of the general practitioner in his every day practice, and the subject matter is limited to diagnosis and treatment. Remaining lectures will be: January 27, Dr. Joseph B. Kirsner, Chicago; February 24, Dr. Willard O. Thompson, Chicago; March 23, Dr. Walter C. Alvarez, Rochester, Minn.; April 27, Dr. Stuyvesant Butler, Chicago, and May 25, Dr. Charles H. Slocumb, Rochester, Minn. All members of the medical profession are invited to attend.

NEW YORK

Assistant Commissioner for Medical Administration.—Dr. Morton L. Levin, Albany, former director, division of cancer control, New York State Department of Health, became assistant commissioner for medical administration October 16. He succeeds Dr. Edward S. Rogers, who resigned last year to become dean of the School of Public Health, University of California, Berkeley. Dr. Levin, a graduate of the University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1930, has been a member of the staff since June 1936. He is president of the Public Health Cancer Association and the Society for the Study of Mass Medicine, an organization founded in 1940 in the state of New York for the purpose of encouraging research in epidemiology and public health.

New York City

Directory of Convalescent Homes.—The sixth edition of the "Directory of Convalescent Homes in the United States" has been issued by the Sturgis Research Fund of the Burke Foundation, White Plains, under the auspices of the Committee on Public Health Relations of the New York Academy of Medicine. The previous edition has long been out of print, and there has been a demand for an up-to-date reference list. The homes are arranged in alphabetical order according to state. Information includes superintendents, types of patients accepted, charges and special therapeutics available.

Laboratory of Toxicology.—The Laboratory of Research Toxicology, initial unit of the recently inaugurated Institute of Industrial Medicine of the New York University-Bellevue Medical Center, has been established under the direction of Rose C. Nelson, Ph.D. Dr. Nelson, former research associate of the Children's Hospital Research Foundation, Cincinnati, and assistant professor of biologic chemistry at the University of Cincinnati, has been named associate professor of industrial medicine. She is a graduate biochemist of the University of Cincinnati and has been active in research in biochemistry.

Interim Quarters for Rehabilitation Institute.—The Institute of Rehabilitation, one of the principal units of the proposed New York University-Bellevue Medical Center, will establish interim quarters January 1 at 325-337 East 38th Street. The move is a result of the generosity of the Milbank Memorial Fund coupled with a $25,000 gift from Bernard Baruch. The institute plans to receive patients as soon as necessary changes are made in the new quarters. Thirty-six dormitory patients at any one time and 150 outpatients a day will be treated in the interim institute, with all eligible except the indigent sick of New York City, now cared for in rehabilitation wards at Bellevue Hospital. Dr. Donald A. Covalt, formerly director of medical rehabilitation for the Veterans Administration and now associate professor of rehabilitation at New York University College of Medicine, will be clinical director. His wife, Dr. Nila K. Covalt, formerly physical therapy director for the Veterans Administration and now assistant professor of physical medicine at the college, will be in charge of physical medicine and Dr. Howard A. Rusk, chairman of the department of rehabilitation, will be director. Patients able to pay suitable fees will finance themselves. By law, persons entitled to rehabilitation in order to earn a living will have their expenses borne by federal grants.

OHIO

Narcotic Violation.—Dr. Arnold M. Landsborough, Garrettsville, was convicted at Cleveland of violation of the Federal Narcotic Law and on October 2 was sentenced to a term of fifteen months.

New Periodical.—A new scientific quarterly published by the faculties of the Colleges of Medicine and Dentistry, Ohio State University, Columbus, began publication December 1. Dr. Allan C. Barnes, chairman, department of obstetrics and gynecology, is editor. The associate editors are: Hamilton B. G. Robinson, D.D.S., Dr. Jonathan Forman and Dr. Charles A. Doan, dean of the College of Medicine. The new periodical is called the *Health Center Journal*.

WEST VIRGINIA

Poliomyelitis Conference.—A state conference on women's activities for the National Foundation for Infantile Paralysis was held in Charleston, December 15, with Mrs. Dale Thomas and Mrs. Fred Sarles as cochairmen. Dr. George Voss of the headquarters office in New York spoke on the work of the national foundation and led a round table discussion on "Your Dimes at Work." Dr. Newman H. Dyer, state health commissioner, presented a paper on "Polio in West Virginia." A motion picture was shown at the luncheon.

Council Recommends Revision of Health Laws.—The council of the West Virginia State Medical Association December 3 unanimously adopted a resolution regarding changes in the state laws pertaining to public health. The council advocates revision of the Medical Practice Act and Public Health Laws to meet changing conditions. It recommends that the distribution and use without charge of serums and vaccines be limited to those unable to pay for them and that patients in state tuberculosis sanatoriums be charged for hospitalization in accordance with their ability to pay. The council recommends the appointment of school physicians for each county or group of counties in the state; the teaching of sex education in public schools, and the organization of a campaign designed to educate

school children to the need for doctors and nurses within the state. It also recommends additional appropriations for local health departments and for the improvement of health facilities in rural areas.

GENERAL

Conference on Physiology of Pregnancy.—A conference on Normal and Pathological Physiology of Pregnancy will be held at the Hotel Pennsylvania, New York, January 30-31 under the sponsorship of the Committee on Human Reproduction, National Research Council, in behalf of the National Committee on Maternal Health. Subjects to be discussed by physicians from all parts of the country include some functional activities of the trophoblast, placental dysfunction in eclamptogenic toxemias, patterns of uterine contractions, the thyroid gland and liver function in pregnancy, endocrine patterns in abortion, nutrition and pregnancy, and toxemia.

American Board Examination.—The American Board of Obstetrics and Gynecology, Inc., announces that the next written examination and review of case histories (Part I) for all candidates will be held in various cities of the United States and Canada, Feb. 6, 1948. Arrangements will be made as far as is possible for candidates to take the Part I examination (written paper and submission of case records) at places convenient for them. Candidates who successfully complete the Part I examination proceed automatically to the Part II examination, to be held May 16-22, 1948, in Washington, D. C. Notice of the exact time and place of the Part I and Part II examinations will be sent to all candidates well in advance of the date of the examination. For further information and application blanks address Paul Titus, M.D., Secretary, 1015 Highland Building, Pittsburgh.

Associate Director of Research.—Theodore E. Boyd, Ph.D., formerly of the Loyola University School of Medicine, Chicago, was appointed December 4 to the newly created position of associate director of research for the National Foundation for Infantile Paralysis. As associate director Dr. Boyd will collaborate with Dr. Harry M. Weaver, director of research, in coordinating the foundation's program of study into the cause, control and treatment of poliomyelitis and allied virus diseases. A native of Ashland City, Tenn., Dr. Boyd received his Ph.D. from the University of Chicago, 1923. He was engaged in research and teaching in physiology at Loyola beginning in 1923 and was made chairman of the department in 1928. Since 1938 the National Foundation for Infantile Paralysis has allocated $6,953,256.66 for such research.

Dr. Powers Receives Borden Award.—Dr. Grover F. Powers, chairman, department of pediatrics, Yale University School of Medicine, New Haven, Conn., was given the Borden Award for "outstanding research in the nutrition of infants and children" at a meeting of the American Academy of Pediatrics in Dallas, December 10. He received a gold medal and a monetary award. Dr. Powers received his medical degree from Johns Hopkins University School of Medicine, Baltimore, in 1913 and was on the staff until 1921. With the exception of one year spent as pediatrician in chief of the Henry Ford Hospital, Detroit, he has been at Yale since 1921. Dr. Powers is president of the American Pediatric Society and a former president of the New England Pediatric Society. The Borden Awards were established in 1936 to recognize and encourage outstanding research achievements in the food industry and related fields. They are administered by seven professional and scientific associations.

Research on Alcoholism.—The Research Council on Problems of Alcohol has submitted an initial grant of $6,000 to the Biochemical Institute of the University of Texas Medical Branch, Galveston, to undertake fundamental research on individual patterns of metabolism in order to determine the possible relation of body processes to susceptibility to alcoholism. This is the second grant made this year by the Research Council to medical schools and their affiliated research hospitals in an effort to unearth the causes of problem drinking and more effective methods of treatment. Early in the year a grant of $30,000 a year for five years was made to Cornell University Medical College-New York Hospital. The Research Council on Problems of Alcohol is carrying on a campaign to obtain funds to sponsor other research in leading medical schools. Research projects on the causes of compulsive drinking are presently planned for New York University-Bellevue Hospital, the University of Illinois, Chicago, and the University of California Medical School, Berkeley-San Francisco.

Association of Blood Banks Formed.—More than two hundred doctors, technicians and administrative assistants in blood center work attended a Blood Bank Institute November 17-19 at Dallas, Texas. The William Buchanan Blood Center of Baylor Hospital sponsored the institute to stimulate better understanding and closer cooperation of blood centers throughout the United States and elsewhere and for teaching newer technics for processing blood for transfusion. As a result of a desire to provide the means for protection in emergencies, the blood bank leaders formed the American Association of Blood Banks as a nonprofit association. G. Albin Matson, Ph.D., Salt Lake City, was elected president; Dr. John Scudder, New York, president-elect; Miss Marjorie Saunders, Dallas, Texas, secretary, and W. Quinn Jordan, Phoenix, Ariz., treasurer. Purposes and methods listed in the constitution are as follows: (1) to promote and foster the exchange of ideas and materials and the dissemination of information relating to blood banking and its technical methodology by education, publicity and research; (2) to foster and plan for cooperation in times of disaster; (3) to function as a clearing house on questions relating to the training of personnel common to such institutions; (4) to keep currently aware of and encourage high standards of service, and (5) to promote and foster and aid and encourage the extension of similar services throughout the United States and its territories.

Red Cross Nurse Enrolment Plan.—The American Red Cross nurse hereafter will be enrolled for service to the community in a new program launched to help meet postwar needs, the American Red Cross national headquarters announced December 7. This marks the first major change in the Red Cross nurse enrolment program since 1909. Before that date contingents of American Red Cross nurses served in disasters and in the Spanish-American War. During World War I the organization recruited 25,000 nurses, of whom 20,000 served with the armed forces and many others in the Home Defense reserves. In World War II 76,425 nurses served with the army and navy.

Ruth B. Reeman, national nursing administrator of the American Red Cross, said: "This new opportunity for service through Red Cross chapters enables nurses to serve more effectively in meeting community needs than is possible through individual action. Qualified professional nurses may serve in their own communities as Red Cross home nursing and volunteer nurse's aide instructors, as well as for service in epidemics, disasters, and in the new Red Cross national blood program. They may also serve on Red Cross chapter committees and in related activities."

The new roster will be made up in each community to meet local needs. Those enrolled prior to the present plans will continue to be recognized as "Red Cross nurses." Acceptance for enrolment and award of the time-honored American Red Cross nurse's badge are based on uniform requirements established nationally by the organization.

Deaths in Other Countries

Dr. Ernst Laqueur, for twenty-seven years professor of pharmacology and director of the Pharmaco-Therapeutical Laboratory, University of Amsterdam, Netherlands, died August 19, aged 67, of heart disease. Professor Laqueur was on the board of editors of the *Acta Brevia Neerlandica* from the time it was founded in 1931 by the Netherlands Society for Physiology and Pharmacology.

Marriages

THOMAS CLAIBORNE GUTHRIE III, Newark, N. J., to Miss Virginia Lee McRae of Rockingham, N. C., November 8.

BERNARD JOSEPH RYAN, New York, to Miss Mary Elizabeth Croken of Schenectady, N. Y., May 17.

CHARLES K. WELLS, Waltonville, Ill., to Mrs. Elizabeth Ava Arenas of St. Petersburg, Fla., June 9.

ALFRED D. BICUNAS, Richmond Hill, N. Y., to Miss Violet E. Freeman of Great Bend, Pa., June 4.

ROBERT GEORGE MARQUARDT to Miss Ann Grace Derr, both of Binghamton, N. Y., September 19.

HUIDEKOPER ROMAINE, Morristown, N. J., to Miss Jacqueline Amelia Lane in Orange, June 14.

THOMAS ALBERT HENSON, to Miss Martha Hipp, both of Greensboro, N. C., August 2.

WILLIAM H. TODD, Chicago, to Miss Marie Hardwig of Little Fork, Minn., October 25.

JOSEPH GREENWALD, Darby, Pa., to Miss Bess Estrin in Philadelphia, October 16.

SAM C. SUGG to Miss Marion Joyce Linton, both of Isola, Miss., October 12.

IRA M. ISRAEL to Miss Muriel Miller, both of New York, October 26.

Deaths

Alanson Weeks ✠ clinical professor of surgery emeritus at the University of California Medical School, died in San Francisco, November 25, aged 70. Dr. Weeks was born in Allegan, Mich., Sept. 15, 1877. Following graduation from the University of Michigan Department of Medicine and Surgery in Ann Arbor in 1899, he went to California, where he became clinical professor of surgery at the University of California Medical School in 1924. During World War I he was chief surgeon of Army Base Hospital number 30, organized for the Red Cross by the University of California. He was awarded the Distinguished Service Medal for "exceptionally meritorious" services during the Marne, St. Mihiel and Meuse-Argonne offensives. Dr. Weeks was a member of the founders' group of the American Board of Surgery, a member of the Pacific Coast Surgical Association and a fellow of the American College of Surgeons. He was chief of surgery at St. Luke's Hospital and consultant in surgery at the Children's, Veterans Administration, Marine and Emergency hospitals. He popularized the intravenous use of dextrose on the Pacific Coast about 1918 and is said to have been the first on the Pacific Coast to perform the Fredet-Ramstedt operation for pyloric stenosis. Dr. Weeks was a genial host, a forthright speaker who hated sham and pretense. His courage and directness were an inspiration to all who knew him.

Harry Milton Conner ✠ Rochester, Minn.; born in Morrison, Ill., May 21, 1881; Kansas Medical College, Medical Department of Washburn College, Topeka, 1909; specialist certified by the American Board of Internal Medicine; member of the Central Society for Clinical Research, Southern Minnesota Medical Association and the Minnesota Society of Internal Medicine; formerly professor of pathology at his alma mater and associate professor of medicine at the University of Minnesota Graduate School; at one time voluntary assistant in pathology, assistant in surgical pathology and first assistant and associate in medicine at the Mayo Clinic; died October 18, aged 66, of bronchopneumonia and postencephalitic parkinsonism.

Oscar Dodd, Evanston, Ill.; born in Rosendale, Wis., Aug. 20, 1864; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1890; member of the American Medical Association, American Academy of Ophthalmology and Otolaryngology and American Ophthalmological Society; fellow of the American College of Surgeons; specialist certified by the American Board of Ophthalmology; served on the staffs of Augustana Hospital in Chicago and the Evanston Hospital; died October 15, aged 83, of uremia and arteriosclerosis.

Harrison Capron Allen, Endicott, N. Y.; New York University Medical College, New York, 1897; member of the American Medical Association; served as school physician in the Endicott schools and at Hooper School in Endwell; died in Owego September 15, aged 76, of coronary sclerosis.

Morris Alleman Birely ✠ Thurmont, Md.; University of Maryland School of Medicine, Baltimore, 1894; director and chairman of the board of the Thurmont Bank; died October 5, aged 75, of cerebral hemorrhage.

Charles Norman Bottum ✠ Marquette, Mich.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1903; twice president of the Marquette-Alger Counties Medical Society; served as president of the Upper Peninsula Medical Society; county health officer; received Selective Service Medal for work during World War II; first medical director of Morgan Heights Sanatorium; on the staffs of St. Luke's and St. Mary's hospitals; died October 6, aged 70, of coronary occlusion.

Leonard Louis Charpier ✠ Midlothian, Ill.; University of Illinois College of Medicine, Chicago, 1922; fellow of the American College of Surgeons; on the staff of the Little Company of Mary Hospital, Evergreen Park, where he died October 3, aged 50, of coronary thrombosis.

Thomas Lyles Davis, Abbeville, S. C.; University of Nashville (Tenn.) Medical Department, 1911; member of the American Medical Association and the Tennessee State Medical Association; served during World War I; at one time practiced in Chattanooga, Tenn., where he was on the staff of Erlanger Hospital; died in Columbia October 1, aged 68, of carcinoma.

John William Donnell, Hudson, Iowa; University Medical College of Kansas City, Mo., 1912; member of the American Medical Association; died in St. Petersburg, Fla., September 27, aged 76, of coronary thrombosis.

James Franklin Earp, La Salle, Mich.; Toledo Medical College, 1902; died in St. Vincent's Hospital, Toledo, Ohio, October 4, aged 74, of hemorrhage due to gastric ulcer.

Charles Emory Ferguson ✠ Washington, D. C.; National University Medical Department, Washington, 1896; served during World War I; died August 14, aged 73, of cerebral thrombosis and generalized arteriosclerosis.

Leland H. Gilleland, Dunedin, Fla.; National Medical College, Chicago, 1899; died August 11, aged 71.

Herschel Gordon Harris, Wilmot, S. D.; Harvey Medical College, Chicago, 1903; Chicago College of Medicine and Surgery, 1904; served during World War I; died October 1, aged 70, of cerebral hemorrhage.

Harry Filmore Kimmel, Derry, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1888; member of the American Medical Association; died September 10, aged 80, of coronary occlusion.

Frederick Augustine King, Marshfield, Mass.; Boston University School of Medicine, 1895; member of the American Medical Association; veteran of the Spanish-American War and World War I; school physician; formerly member of the board of health in Boston; assistant surgeon at Goddard Hospital in Brockton; died in the Veterans Administration Hospital, West Roxbury, September 14, aged 78, of arteriosclerotic heart disease, cerebral hemorrhage and a fracture of the right femur.

Samuel L. Le Vine, Chicago; Illinois Medical College, Chicago, 1909; for many years attached to the city health department; died in the Illinois Masonic Hospital October 7, aged 63, of metastatic carcinoma of the lungs.

Nat B. McCormick, Millington, Tenn.; Memphis Hospital Medical College, 1888; died in St. Joseph's Hospital, Memphis, September 1, aged 87, of carcinoma of the lung.

Leopold Marcus, Miami Beach, Fla.; Columbia University College of Physicians and Surgeons, New York, 1896; died August 24, aged 71.

James Robert Martin, Houston, Texas; Baylor University College of Medicine, Dallas, 1933; interned at the Hotel Dieu in Beaumont; formerly a resident in urology at the Grasslands Hospital in Valhalla, N. Y.; served in the medical corps of the U. S. Naval Reserve during World War II; member of the American Medical Association; found dead in bed, September 2, aged 39.

Wayne Parry Mecklem, Mansfield, Ohio; University of Wooster Medical Department, Cleveland, 1910; served during World War I; member of the city health department; on the staff of Mansfield General Hospital; died in Veterans Administration Hospital in Cleveland August 12, aged 61, of heart disease.

George Wendell Phillips, Sayre, Okla.; Tennessee Medical College, Knoxville, Tenn., 1901; died September 1, aged 70, of heart disease.

James Stuart Plant ✠ Newark, N. J.; University of Pennsylvania School of Medicine, Philadelphia, 1918; specialist certified by the American Board of Psychiatry and Neurology, Inc.; member of the American Psychiatric Association; served as chairman of the executive committee of the National Committee for Mental Hygiene; director of the Essex County Juvenile Clinic; author of "Personality and the Cultural Pattern"; died September 7, aged 57, of coronary occlusion.

Mendel Poliak, Springfield, Mass.; Université de Montpellier Faculté de Médecine, France, 1922; member of the American Medical Association; on the staff of Wesson Memorial Hospital, where he died September 15, aged 60, of congestive heart failure.

Henry Francis Quinlan, Dalton, Mass.; University of the City of New York Medical Department, 1890; died in St. Luke's Hospital, Pittsfield, September 22, aged 86, of cerebral hemorrhage.

Arthur Hermann Rohlfing, St. Louis; Washington University School of Medicine, St. Louis, 1904; member of the American Medical Association; on the staff of Bethesda General Hospital; died September 14, aged 64, of heart disease.

Grover Melton Saunders Roof, Columbia, S. C.; Medical College of the State of South Carolina, Charleston, 1924; member of the American Medical Association; died in Baptist Hospital September 7, aged 52, of carcinoma of the lung.

Bertha E. Sutton Sheetz, Trenton, Mo.; College of Physicians and Surgeons, Medical Department Kansas City University, Kansas City, Kan., 1901; member of the American Medical Association; on the staff of Wright Memorial Hospital; died September 2, aged 68, of heart disease.

David Franklin Smith, Esto, Fla. (licensed in Florida, year unknown); died September 3, aged 76, of senility.

Albert John Struble, Centerville, S. D.; Barnes Medical College, St. Louis, 1900; died August 25, aged 75, of injuries received in an automobile accident.

J. Pitt Tomlinson, Lake Wales, Fla.; Southern Medical College, Atlanta, 1898; member of the American Medical Association; past president of the Bradford County Medical Society; died September 7, aged 73, of cerebral hemorrhage.

James Travis Vance, Coronado, Calif.; University of California Medical School, San Francisco, 1927; began active duty as a lieutenant in the medical corps of the U. S. Naval Reserve in February 1941; promoted to commander; died in the Naval Air Station, Pomona, June 5, aged 49, of coronary thrombosis.

Edwin Wachlin, Apple River, Ill.; Loyola University School of Medicine, Chicago, 1919; served during World War I; died in St. Francis Hospital, Freeport, September 1, aged 55, of hypertension and nephrolithiasis.

Charles Henry Weber, Santa Barbara, Calif; University of Pennsylvania Department of Medicine, Philadelphia, 1896; formerly on the faculty of the Medico-Chirurgical College, Graduate School of Medicine, University of Pennsylvania in Philadelphia, where he served as medical director of the Juvenile Court and on the staffs of Episcopal and Children's hospitals; served during the Boer War and in France during World War I; died in Cottage Hospital September 30, aged 74, of heart disease.

William B. Westcott, Montgomery, Ala.; Columbia University College of Physicians and Surgeons, New York, 1902; member of the American Medical Association; on the staffs of Hubbard and St. Margaret's hospitals; died September 14, aged 69, of cerebral hemorrhage.

Joseph Hosphmer Wheat, Chicago; Loyola University School of Medicine, Chicago, 1918; served on the staff of Illinois Masonic Hospital; died September 15, aged 65, of carcinoma.

Frank Livingston Whelpley ✠ Goldsboro, N. C.; Washington University School of Medicine, St. Louis, 1902; specialist certified by the American Board of Psychiatry and Neurology, Inc.; member of the North Carolina Eugenics Board and the American Psychiatric Association; since 1918 connected with the State Hospital, where he had been superintendent for many years, retiring in 1946; died September 7, aged 74, of cerebral hemorrhage.

James Edwin Wolfe ✠ Wichita, Kan.; University of Kansas School of Medicine, Kansas City, 1920; fellow of the American College of Surgeons; president-elect of the Sedgwick County Medical Society and the Kansas Public Health Association; director of public health and formerly director of public welfare; on the staffs of St. Francis and Wesley hospitals; died September 15, aged 53, of coronary occlusion.

Robert Ulyses Zimmerman ✠ Lexington, N. C.; Davidson School of Medicine, 1901; died August 16, aged 70.

CAPT. LEWIS T. STONEBURNER III
M. C., A. U. S., 1913-1944

CAPT. STANLEY J. SNITOW
M. C., A. U. S., 1917-1944

LIEUT. ARNOLD H. WARSHELL
M. C., A. U. S., 1914-1944

KILLED IN ACTION

Lewis Tilghman Stoneburner III, Richmond, Va.; born in Richmond March 2, 1913; Medical College of Virginia, Richmond, 1937; diplomate of the National Board of Medical Examiners; served an internship and residency at the Boston City Hospital; member of the American Medical Association and the Richmond Academy of Medicine; an associate of the American College of Physicians; served as a fellow at the Thorndike Research Laboratory and assistant in medicine at Harvard University in Boston, an instructor in medicine at his alma mater and assistant physician to its hospitals; a member of the medical staff of Sheltering Arms Hospital; became affiliated with the then inactive 45th General Hospital organized at the Medical College of Virginia; began active duty as a captain in the medical corps, Army of the United States, in May 1942; attended the Army Medical School; in March 1943 went to North Africa; detached from the 45th General Hospital and attached to the office of medical consultant, North African Theater of Operations; later assigned as a hospital inspector; in October 1943 boarded a B-25 bomber on a flight from Algiers to Tunis to visit hospitals in that vicinity; reported missing in action; declared dead Oct. 11, 1944, aged 31.

Captain Stanley J. Snitow's obituary appeared in THE JOURNAL, October 18, page 446.

Arnold Harris Warshell, Chicago; University of Illinois College of Medicine, Chicago, 1939; interned at Bethesda Hospital in Cincinnati and formerly resident on the staff of St. Luke's Hospital in Milwaukee; when the National Guard of Illinois was federalized in February 1941, became a private in the medical detachment of the 122d Field Artillery Battalion of the 33d Division; became first lieutenant in the medical corps, Army of the United States, in September 1941; served overseas in the Philippines; a short time after the bombing of Pearl Harbor, and for a year and a half thereafter, officially listed as "missing in action"; killed in the South China Sea Oct. 24, 1944, aged 30, when a Japanese ship on which he was being transported while a prisoner of war was sunk.

Foreign Letters

LONDON

(From Our Regular Correspondent)

Nov. 15, 1947.

The End of the Indian Medical Service

The end of the Indian Medical Service was briefly reported in a previous letter to THE JOURNAL (October 11, page 371). This has taken place without any ceremony or expression of gratitude for the introduction and establishing of modern medicine in that vast subcontinent, inhabited by many races speaking many languages. Yet Hindus, women as well as men, come in numbers to London to be taught in its medical schools. The only communications received from the new government by most of the medical officers of the Indian Medical Service, including those who offered to serve for another year, were curt notices of dismissal. At a meeting of the medical officers in 1945 it was agreed that the time had come to transfer the burden of responsibility to Indian hands. Their ability to maintain the high standards of the service was thought by some to be shown by their eagerness to assume control. Only the undignified termination was regretted.

A meeting to discuss the change was held in London and was addressed by Dr. R. G. Cochrane, Principal of the Mission Medical College, Vellore, Madras. He expressed the opinion that scientific standards are threatened by the pull of Eastern medicine. A proportion of Indians have an aptitude for scientific work, he said, but in institutions research is apt to be lost by lack of staff. Moreover, many Indians are strangely attracted by Ayurvedic medicine, which is worse than the medicine of the Middle Ages in Europe; he agreed with Sir Philip Manson-Bahr, however, that the study of its remedies should go on.

Of the great value of the researches of the Indian Medical Service, particularly in tropical medicine, it is not necessary to speak. But the outstanding discovery by Ross of the cycle known by his name—the development of the Plasmodium malariae in the mosquito—may be mentioned. It is interesting to recall that the officers of the Indian Medical Service did valuable work outside their profession. In the early days they undertook various kinds of work for which scientific knowledge was required, because technicians were not available. They acted as postmasters, conservators of forests and cotton agents. One conducted the experiments for the introduction of the electric telegraph into India.

The Empire Medical Advisory Bureau

The Council of the British Medical Association has decided to establish an Empire Medical Advisory Bureau for practitioners visiting Britain, particularly those from the dominions and colonies. The main objects are to make information available as to facilities for postgraduate study, to maintain a register of hotel accommodation, to arrange private hospitality and to provide a wide range of general information, including facilities for sport, travel and entertainment. A medical director is to be appointed to the official staff of the association, who will be responsible, under the committee of management, for the general organization and administration of the bureau. Office accommodation and a clerical staff will be provided at British Medical House. Candidates for the position of medical director must be registered medical practitioners with considerable organizing and administrative ability. The salary for the post will be between $6,000 and $8,000 per annum according to the qualifications and experience of the applicant appointed.

Medical Association Protests Against Tax on Drugs

To close the huge gap between imports and exports, which is an obsession of our statesmen and people, the Chancellor of the Exchequer has proposed increases of our already heavy taxation. One of his proposals—the increased purchase tax on many classes of drugs—has given rise to a protest to the Ministry of Health by the British Medical Association. It is impossible, says the association, for any doctor with the interest of his patients at heart to view other than with grave concern any measure which increases the cost of sickness or adds to the anxiety which accompanies it. Many of the drugs affected by the increase are in constant use. The association points out that substantial increase in the cost of these medicines is bound to be reflected in increased cost of medical services, which will fall most heavily on the chronically sick, to whom, perhaps more than any other section of the community, the additional burden will cause hardship.

Free Hearing Aids

A two piece hearing aid, designed and tested by the electro-acoustics committee of the Medical Research Council, is being manufactured for free distribution by the Government. It is evidently part of the program "Free Medical Treatment for All." At present many expensive hearing aids are extensively advertised by their proprietors. In reply to a question in the House of Commons, Mr. H. Morrison, a member of the Government, said that models of the new aids had been tested at clinics in London and Manchester on 27 persons with various degrees of deafness and well practiced in the use of aids. Comparison was made in each case with the patient's own previously used aid, and also with a highly recommended American instrument. Twenty of the patients heard best with the new aid, and three others equally well. All the patients commented on the new aid's exceptionally good reproduction and preferred it on that account.

PALESTINE

(From Our Regular Correspondent)

JERUSALEM, Nov. 15, 1947.

Cholera in Egypt—Protective Measures in Palestine

The first case of cholera in the epidemic in Egypt was notified on Sept. 23, 1947. The number of deaths and new cases reported were continuously on the increase until the beginning of November, the peak having probably been reached with over 500 deaths and more than 900 new cases reported in one day. A total of 7,897 deaths were reported up to November 1. The actual number of deaths is probably much higher, as pointed out by the Egyptian health authorities, because the peasants hide their sick rather than report them to the health authorities.

Fighting cholera has been heroic work for the Egyptian health organizations and for the physicians. Since November the epidemic has been decreasing, about 60 deaths and more than 100 new cases being reported daily. For the first time in the history of cholera, airplanes were used, large districts being sprayed with D. D. T. (4,4'-dichlorodiphenyltrichloroethane). An interesting development was the fighting of cholera with a new sulfonamide derivative brought to Egypt by Dr. Harry T. Seneca, of the College of Physicians and Surgeons of Columbia University, New York. The drug had been discovered recently at a New Jersey chemical research institute and successfully used in laboratory tests.

In October a symposium on cholera was held by the Association of Jewish Physicians in Jerusalem. The cholera epidemic in Egypt gave rise to the apprehension that Palestine might be endangered, bordering Egypt closely to the south. The symposium was called to learn what the Palestine government had done to protect the country and what was left undone, as well as how the Jewish institutions might cooperate. A number of leading physicians, who had in the Army seen cholera in other countries, participated in the reports and suggestions.

Dr. A. Steinitz and Dr. Grushka reported on their experiences in Burma and in the Balkans. Professor W. Strauss spoke on the value of preventive vaccination against cholera. In the south of Palestine, in the so-called Negev, there is prac-

tically no water. The Negev is a desert only now coming slowly under cultivation. Professor Strauss did not see, therefore, a direct threat to Palestine from Egypt through the southern border. He expressed the opinion that the epidemic will flare up in Palestine only after having ended in Egypt, as the borders will then reopen on all sides and most of the bacilli carriers will then gain entrance to Palestine through the Syrian and Transjordan borders. The water will be contaminated over the same route, and that means, of course, source of infection and danger. As far as known, the protection afforded by vaccination lasts about three months. Once vaccination is begun, it must be continued every three months. Dr. W. Silberstein, who prepares the cholera vaccine for the Palestine government, reported on the history of vaccination.

Opinion differed as to how many vibrios should be given. Olitzki, of the Bacteriologic Department of the Hebrew University, proposed a high amount, as the effective O antigen is about ten times weaker in the cholera vibrios than in typhoid bacilli. Olitzki expressed the belief that a concentration of 20 billion vibrios should be right. However, since severe general reactions are to be expected from this amount, he advised at least 5 billion vibrios per cubic centimeter. This concentration is contained in the vaccine made by Dr. Lewin, of Strauss Health Center. The official vaccine issued by the government contains only 3 billion vibrios. Olitzki is of the opinion that a polyvalent vaccine is best. It is strange that no fresh cholera strain could be obtained from Egypt for the preparation of the vaccine; neither the Hebrew University's nor the Palestine government's wishes for fresh strains have been complied with by the Egyptian government.

National Conference on Nutrition

In October, the fourth national conference on nutrition took place in Tel-Aviv. The conference was called by the Nutrition Committee of the Jewish Agency. Dr. K. Guggenheim opened the conference with a report on "The Modern State and Its Task in the Field of Nutrition." This report and the lecture of Professor Rosenbaum on "Recent Progress in the Science of Nutrition" were followed by discussions. The two hundred and fifty participants in the conference testified to the great interest aroused by questions of nutrition. A special meeting was held for the discussion of protein nutrition, a problem that is extremely important for Palestine. Many reports were based on original research done by the Economic Institute of the Jewish Agency (Bonne), the Nutritional Department of the Strauss Health Center, Jerusalem (Bawly), and the Department of Hygiene of the Hebrew University (Buechler, Reinitz, Rabinowitz and Guggenheim).

ITALY

(From Our Regular Correspondent)

NAPLES, Oct. 26, 1947.

The National Congress of Medicine and Surgery

The 1947 National Congress of Medicine and Surgery, the second convened since the war, was held in Rome in October. This congress was much more impressive than that held last year at Florence.

Streptomycin

The main interest of the conference was the presentation before a large audience of a number of patients who had recovered from tuberculous meningitis following treatment in the Forlanini Sanatorium in Rome, Italy's most important sanatorium. The treatment, involving the use of streptomycin, was described by Professor Omodei-Zorini, director of the sanatorium. Professor Cocchi, director of the pediatric clinic of Florence University, then described the use of streptomycin and sulfonamide drugs in the treatment of tuberculosis in infants. Hundreds of roentgenograms were shown to illustrate the stage of the disease, the progress of improvement with treatment and final complete recovery. The cases included grave miliary tuberculosis in children below the age of 12 years. The demonstrations greatly impressed the assembly, which, owing to the large number of persons present, had to be transferred from the medical clinic to the "Aula Magna" of the University.

Success in using the drug depends on the amount of streptomycin given, and on the adjustment of the dose to the case. The amount of streptomycin used should be about 1 Gm. a day: overdosage should be avoided, otherwise the effects may be harmful.

A much appreciated lecture on streptomycin was given by Dr. Harrell in the Naples Piedmont Sanatorium in September, shortly after the International Congress in London. His lecture was attended by the chancellor of the university and many other scientists. Visits by American doctors and their cordial relations with Italian doctors have created most favorable impressions. This was particularly apparent in Rome, at the congress, at which subjects of interest in medical circles of both America and Italy came under discussion.

The Mediastinum

One subject, the physiopathology of the mediastinum, was discussed by both the medical and surgical sections. For the surgical section, Professor Dogliotti, director of the Turin surgical clinic, spoke of the success of American surgery in relation to the mediastinum. He described his observations during a recent journey to the United States, where he had been a guest of American colleagues. Apart from a difference in operative technic, Dogliotti was impressed by the rigorous aseptic measures adopted in the operating rooms and the measures taken to insure the maximum of care in handling patients both before and after the operation.

Speaking for the medical section, Professor Condorelli, director of the medical clinic of Catania University, was of the opinion that any interference with the functions of the mediastinum would result in morbid repercussions. Lesions of the mediastinal lymph glands or the aorta result in a reduction of the mediastinal cellular tissues which are necessary to stabilize the continuity of contact between one organ and the next. Since the mediastinum influences the rhythm of the respiratory motion, cellulitis of the mediastinum will almost certainly result in a chronic effect on the venous vessels. Alteration of the elasticity of the mediastinal tissues can produce a slowing down of the backward flow of venous blood toward the heart.

Other Topics

Numerous other topics were discussed, including the surgery of the esophagus, surgical treatment of cancer of the prostate and new approaches to thyroid diseases. Surgery in tuberculosis was discussed again at the congress in Milan on November 30 to commemorate the birth of Forlanini in 1847.

Among those who presided at the Rome Congress was Professor Raffaele Bastianelli, the noted surgeon of Italy, a friend of Cushing; Professor Frugoni, president of the Società Nazionale di Medicina, and Professor Giordano of Venice.

After the congress ended, Dr. Mario Musella spoke to the Italian medical world over the Rome radio about the significance of this congress, which involved thousands of the country's medical men, in the work of reconstruction in which medicine and surgery were taking a leading part in the intellectual field. Following Dr. Musella on the radio, Dr. Mayer, secretary general of the Belgian Surgeons Society, spoke on the productive work of Italy, which in taking up again in full its old traditions was showing the important part Italy has had in the development of medical knowledge.

In the library exhibit at the congress, the new book by Dr. Morris Fishbein, "A History of the American Medical Association," was appreciated with many other books and medical magazines. The next National Congress of Medicine and Surgery will be held at Bologna in 1948.

TURKEY

(From Our Regular Correspondent)

ANKARA, Oct. 7, 1947.

Specialization in Turkey

After an investigation by a committee, the Ministry of Health determined and announced the branches of medical specialities in regulations published in 1929. Experience of almost twenty years showed the need to amend the 1929 regulations. As a result a new eighteen paragraph regulation concerning medical specialists has been prepared by the Ministry of Health, investigated and endorsed by the Council of State and on the decision of the Council of Ministers was published in the Official Gazette Aug. 9, 1947.

According to this regulation there are twenty-two specialities: internal medicine, pediatrics, bacteriology and infectious diseases, parasitology, nervous and mental diseases, legal medicine and psychology, radiology, general surgery, neurosurgery, stomatology, child surgery and orthopedics, gynecology and obstetrics, urology, dermatology and venereal diseases, otorhinolaryngology, ophthalmology, physical therapy and hydrology, pathologic anatomy, pharmacodynamics, hygiene, chemical biology and public health. A three year internship is required for specialization in ten branches: internal medicine, pediatrics, general surgery, neurosurgery, gynecology and obstetrics, urology, orthopedics, stomatology, bacteriology and infectious diseases and hygiene; for the rest only two years are required.

The requirements for an internship are: qualification to enter the Turkish civil service and ability to read, write and translate from English, German, French or Italian. Candidates must have successfully passed the competitive examination with the grade "very good" or at least "good" at the medical school. Applicants who have passed the foreign language examinations held for civil servants twice a year are exempt from the language examinations. According to the former regulation there were two classes of specialists. Second class specialists could not obtain appointments in government or municipal institutions; they could only engage in private practice. This second class has now been eliminated. Twice a year a confidential report on the work of the intern is sent to the Ministry of Health. Interns having twice received an unsatisfactory note from their teacher are obliged to discontinue the internship. At the completion of the three years the intern has to write a thesis and if it has been accepted has to pass a theoretic and practical examination before a jury. Interns whose thesis has been rejected spend another year at the internship and write another thesis.

Provincial governors and health officers are informed by circular of the number of interns required for hospitals and other institutions. The Ministry of Health decides on the appointments of civil and military resident internships. University clinics and laboratories, government general and model hospitals and institutions affiliated with the military medical academy are the principal centers for the training of specialists.

For public health officers the Ministry of Health provides special preparation in hospital clinics and at the Central Institute of Hygiene. They get practice in preventive as well as curative medicine, and practice in health centers; they will get appointments in health centers the number of which is to be increased in the near future. Public health has been the latest to be added to the speciality list in Turkey.

To obtain an internship it is necessary to have completed the obligatory government service; those who are not under such obligation must have completed their service at the military medical academy in accordance with the reserve officer's law, or must have spent at least two years in the government health organization. Only those who specialize in public health have the years of their special preparation deducted from their obligatory governmental service.

Physicians who have had their specialist preparation at an accepted hospital or laboratory in a foreign country, producing a recognized certificate, and have spent on their preparation the required time stated in the Turkish regulation have to undergo an examination before the jury of the medical school. Having satisfied the examiners the applicant receives the Turkish specialist certificate which is forwarded to the Ministry of Health for registration.

Specialists desiring to change over to another branch of their speciality need spend on their preparation only half or two thirds of the time indicated in the regulation.

Because the country is agricultural and the number of physicians is insufficient, the location of the health centers will largely be in rural communities. The health officer must be given ample practice in hospitals to enable him to deal with difficult deliveries, minor operations, circumcisions, diseases of children, to know how to use an x-ray machine and to deal with fractures and dislocations. Because many communities are without dentists the health officer should know how to pull a tooth and give dental first aid.

Penicillin Therapy

Dr. Halil Çiray, director, department of obstetrics and gynecology, Ankara General Hospital, has published his 1946 observations regarding penicillin therapy. Of 56 cases in which penicillin was used 48 involved complications after deliveries or after gynecologic operations and 8 were septic deliveries and septic absorptions. Four patients died, 1 of a pulmonary complication following a cesarean operation; 1 patient died of peritonitis due to inflammation of the adnexa; 1 patient admitted in a moribund condition died four days later of cancer of the cervix, and 1 patient died of a colon bacillus infection ten days after a prolapse operation. The percentage of recovery in these serious cases with much fever was 92.9, and the death rate 7.1 per cent. Omission of the last 2 cases would indicate a still lower death rate.

Penicillin was used in the following cases: 4 septic deliveries and 4 septic abortions, 4 artificial deliveries, 2 artificial deliveries complicated by inversion, 1 inversion, 2 forceps deliveries, 10 cesarean deliveries, 5 myomas, 4 prolapses, 2 prolapses and ligamentopexies, 2 ligamentopexies, 4 ligamentopexies and appendectomies, 1 ovarian cyst, 1 ovarian cyst and appendectomy, 3 adnexopexies, 3 adnexopexies and appendectomies, 1 case of hydrosalpinx, 1 case of suppurative oophoritis, 1 cancer of the uterus, 2 cancers of the cervix and 1 extrauterine pregnancy.

According to the severity of the cases, from 200,000 to 600,000 units per dose were given from three to five days, and in some cases a total amount of 2,800,000 to 5,000,000 units of penicillin was given with no untoward results.

The penicillin used was the product of different American laboratories. Not until toward the end of 1945 did penicillin enter Turkey in any larger quantities. In view of the scarcity the distribution of penicillin was under the supervision of the Ministry of Health. Only specialists could obtain it and only on a written request indorsed by the Ministry of Health. This first American penicillin had been procured through the Turkish Red Crescent Society. Because of transportation difficulties some of the shipments of penicillin had been detained in Egypt for a long time and had deteriorated in transit. In 1946-1947 penicillin began to arrive in quantities sufficient to enable its wide application in hospitals; the sale of penicillin is now unrestricted. From 1943 to 1945 a detailed report was required of each case in which American penicillin was used, to make sure that penicillin would not find its way into the black market. To prevent its use for the treatment of venereal diseases each report was carefully investigated by the Ministry of Health and a penalty was imposed on those giving a false report. Telegraphic demands from other parts of the country often had to be refused because there was none available. When available again it was given out in the order of priority. For the Ministry of Health the distribution of penicillin was a troublesome affair for these years.

Correspondence

SCHISTOSOMIASIS

To the Editor:—Schistosome ova appearing in the excreta after a course of treatment are often attributed to reinfection rather than to an incomplete cure, though early Japanese investigators found it impossible to reinfect some animals in which the parasites had died out.

On only one occasion have I had reason to believe that fresh infection has occurred with Schistosoma hematobium after a complete course of antimonium potassium tartrate has been administered, and it is possible that the natural death of schistosomes may produce the same immunity.

This salt is sometimes supposed to be more toxic than its less stable sodium equivalent, but when it is dissolved in boiling water and passed through filter paper while still hot, the tendency of the patient to cough and vomit is avoided. An injection of 1 Gm. may well be regarded as the maximum.

F. GORDON CAWSTON, M.A., Durban, South Africa.

EFFECT OF FLUORIDES IN DRINKING WATER ON TEETH

To the Editor:—In the reply to Dr. G. P. Joseph in the October 11 issue of THE JOURNAL, page 397, it is stated that "the fluorine content of the domestic water used by the mother during gestation is immaterial." I would like to point out that it may be very material.

From dental surveys that I conducted in different parts of South Africa it was found that the deciduous teeth of children whose mothers drank water containing up to 10 parts per million of fluorine during gestation and lactation were remarkably free from caries and were not mottled. From my experimental investigations with albino rats, I found that in rats whose mothers were given 100 parts per million of fluorine in the drinking water during gestation and lactation there developed considerably less caries than in rats whose mothers did not receive fluorine. These young rats were placed after weaning on a standard caries-producing diet without any fluorine for eighty days. The rats showed no mottling of the incisors, which would indicate that very little fluorine is transmitted through the placenta and the milk. The ingestion of fluorine during gestation and lactation may result in the formation of highly caries-resistant teeth in the child. It must first be determined what amount will be harmless to the mother and not cause mottling of the permanent teeth of the child. Most of the fluorine will be excreted in the urine, but small amounts will be deposited in the bones of the mother and the fetus. Optimum amounts of fluorine would appear to be withdrawn during calcification of the teeth, making them more caries-resistant.

It may be mentioned that the diet of the mothers who drank up to 10 parts per million of fluorine was high in protein, consisting mainly of meat (mutton) and bread. My experimental investigations showed that rats whose mothers were placed on a high protein diet during gestation and lactation had considerably less caries than rats whose mothers were placed on a low protein diet. Furthermore, in rats whose mothers were placed on a high protein diet and 100 parts per million of fluorine in the drinking water during gestation and lactation, there developed practically no caries. These young rats were placed after weaning on a standard caries-producing diet without any fluorine for eighty days. It was recently found that the incidence of caries among soldiers coming from the ranching states of Texas, New Mexico, Wyoming and Montana was less than half that among soldiers coming from Maine, Rhode Island, New York and New Jersey. More proteins and fluorine are probably ingested in these meat-producing states than in the Northern states mentioned. From these observations, the ingestion of fluorine in nontoxic quantities and a high protein intake during gestation and lactation may prove extremely effective in reducing the high incidence of caries in the future and may serve a better purpose than adding fluorine to communal water supplies.

T. OCKERSE, D.M.D., D.D.S., Pretoria, South Africa.
Dental Health Officer, Department of Health.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

NATIONAL BOARD OF MEDICAL EXAMINERS EXAMINING BOARDS IN SPECIALTIES

Examinations of the National Board of Medical Examiners and the Examining Boards in Specialties were published in THE JOURNAL, Dec. 20, page 1092.

BOARDS OF MEDICAL EXAMINERS

ALABAMA: *Examination.* Montgomery, June 22-24. 1948. Sec., Dr. D. G. Gill, 519 Dexter Ave., Montgomery 4.

CALIFORNIA: *Oral.* San Francisco, Jan. 17-18; Los Angeles, Feb. 28-29. *Written Examination.* Los Angeles, March 1-4. *Oral and Clinical Examination for Foreign Graduates.* Los Angeles, Feb. 29; San Francisco, June 6. Sec., Dr. Frederick N. Scatena, 1020 N Street, Sacramento 14.

CONNECTICUT: * *Examination.* March 9-10. Sec., Dr. Creighton Barker, 258 Church St., New Haven. *Homeopathic Examination.* Derby, March 9-10. Sec., Dr. J. H. Evans, 1488 Chapel St., New Haven.

DELAWARE: *Examination.* Dover, Jan. 13-15. *Endorsement.* Dover, Jan. 20. Sec., Dr. J. S. McDaniel, 229 S. State St., Dover.

HAWAII: *Examination.* Honolulu, Jan. 14-15. 1948. Sec., Dr. S. E. Doolittle, 881 S. Hotel St., Honolulu, T. H.

IDAHO: Boise, Jan. 13-15. Sec., Miss Estella S. Mullner, 355 State House, Boise.

ILLINOIS: Chicago, Jan. 6-8. Supt., Dept. of Registration and Education, Mr. Fred W. Ruegg, Springfield.

INDIANA. *Examination.* Indianapolis, June 1948. Sec., Board of Medical Registration and Examination, Dr. Paul R. Tindall, K. of P. Bldg., Indianapolis.

KENTUCKY: *Examination.* Louisville, June 16-18. Sec., Dr. P. E. Blackerby, 620 S. 3d St., Louisville.

MINNESOTA: * Minneapolis, Jan. 20-22. Sec., Dr. J. F. DuBois, 230 Lowry Medical Arts Bldg., St. Paul 2.

MISSISSIPPI: Jackson, June 1948. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson.

MISSOURI *Examination.* Kansas City, Jan. 19-21. Exec. Sec., Mr. John A. Hailey, P. O. Box 4, State Capitol Bldg., Jefferson City.

NEBRASKA: * *Examination.* Omaha, Dec. Dir., Bureau of Examining Boards, Mr. Oscar F. Humble, 1009 State Capitol Bldg., Lincoln.

NEW HAMPSHIRE. *Examination.* Concord, March 11-12. Sec., Board of Registration in Medicine, Dr. John S. Wheeler, 107 State House, Concord.

NEW JERSEY: *Examination.* Trenton, June 15-17. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NEW YORK: *Examination.* Albany, Buffalo, New York, Syracuse, Feb. 16-19. Sec., Dr. J. L. Lischner, Jr., Education Bldg., Albany.

NORTH CAROLINA. *Endorsement.* Pinehurst, Jan. 12. Sec., Ivan Procter, 226 Hillsboro St., Raleigh.

NORTH DAKOTA: Grand Forks, Jan. 6-9. Sec., Dr. G. M. Williamson, 4½ S. Third St., Grand Forks.

OHIO: *Endorsement.* Columbus, Jan. 6. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus 15.

OREGON: * *Examination.* Portland, Jan. 21-23. Final date for filing application is Jan. 7. *Endorsement.* Portland, Jan. 23-24. Final date for filing application is Jan. 9. Admin., Board of Higher Education, Miss L. M. Conlee, Univ. of Oregon, Eugene.

PENNSYLVANIA: *Examination.* Philadelphia, Jan. 13-16, 1948. Acting Sec., Board of Medical Education and Licensure, Mrs. M. G. Steiner, 351 Education Bldg., Harrisburg.

RHODE ISLAND: * *Examination.* Providence, Jan. 8-9. Chief, Div. of Prof. Regulation, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH DAKOTA: * Pierre, Jan. 20. Sec., State Board of Health, Dr. Gilbert Cottam, Capitol Bldg., Pierre.

UTAH. *Examination.* Salt Lake City, June, 1948. Asst. Dir., Department of Registration, Miss Rena B. Loomis, 324 State Capitol Bldg., Salt Lake City.

WASHINGTON: * *Examination.* Seattle, Jan. 19-21. Sec., Dept. of Licenses, Miss Virginia Wotherspoon, Olympia.

WEST VIRGINIA. Charleston, Jan. 12-14. Comm., Public Health Council, Dr. N. H. Dyer, State Capitol, Charleston 5.

WISCONSIN: * *Examination.* Madison, Jan. 13-15. *Reciprocity Oral.* Madison, Jan. 14. Sec., Dr. C. A. Dawson, Tremont Bldg., River Falls.

WYOMING: *Examination.* Cheyenne, Feb. 2. Sec., Dr. G. M. Anderson, Capitol Bldg., Cheyenne.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

IOWA: Des Moines, Jan. 13, April 13, July 13, Oct. 12. Sec., Dr. Ben H. Peterson, Coe College, Cedar Rapids.

MICHIGAN: *Examination.* Ann Arbor and Detroit, Jan. 9-10. Sec., Miss Eloise LeBeau, 101 N. Walnut St., Lansing.

MINNESOTA: *Examination.* Minneapolis, Jan. 6-7. Sec., Dr. Raymond N. Bieter, 105 Millard Hall, Univ. of Minnesota, Minneapolis 14.

NEBRASKA: *Examination.* Omaha, Jan. 13-14. Dir., Dept. of Health, Mr. Oscar F. Humble, Room 1009, State Capitol Bldg., Lincoln 9.

OKLAHOMA. Spring 1948. Sec., Dr. Frank Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

TENNESSEE: *Examination.* Memphis, Dec. 30-31. Sec., Dr. O. W. Hyman, 874 Union Ave., Memphis.

WASHINGTON: *Examination.* Seattle, Jan. 14-15. Sec., Dept. of Licenses, Miss Virginia Wotherspoon, Olympia.

Miscellany

AN UNDERPOPULATED MEDICAL SPECIALTY: HOSPITAL ADMINISTRATION

CLAUDE W. MUNGER, M.D.
New York

The medical graduate in seeking a career too seldom thinks of hospital administration. Yet, as a medical specialty, it offers opportunity for the deep satisfaction of usefulness to society and tangible rewards which fully justify its consideration. The average physician who has devoted ten years or more to preparation for the practice of medicine is likely to feel that his future is inextricably tied to the clinical practice of his profession. He has permitted himself to take a clinical career for granted to the extent that not often enough does he undertake to survey fully the whole field of usefulness open to the well trained physician.

Every modernly educated physician who is the product of a top-grade medical college has been schooled to the highly important function which the hospital plays not only in medical education but in the successful practice of medicine. If he has been alive to current thought about the present and in particular the future development of medical practice, he cannot have failed to realize the focal position of the hospital in the whole scheme of medical care, whatever ideologies may pertain in medical practice of the future. Thus far he has seldom thought of himself as contributing to medical care through administering these medical institutions, which more and more are the keystones of medicine itself.

The American hospital system has undeniably grown to be the greatest and the best in the world. Before the recent war no nation could match the record of this country in hospital development, but that prewar achievement was scarcely more than a good sample of the growth in hospitals which is now under way and which is certain to entail expansion to an extent unthinkable even in the recent past.

The hospital offers outstanding opportunity to the physician who is willing to and capable of applying his professional knowledge, through administrative avenues, to the shaping and guiding of hospital performance. Knowledge and application of administrative technic will be scarcely less important than his knowledge of medicine, but these skills, used in combination, offer a man an unlimited chance to influence and assist his own profession toward its ultimate usefulness.

There are[1] now some 6,500 hospitals on the registry of the American Medical Association. Many of them are small, without enough administrative problems to occupy the interest and the time of a physician-administrator, except as far as there is a growing tendency for physician-administrators to act in a consulting or general supervisory capacity over groups of such institutions. On the other hand, of 4,744 general hospitals of all sizes there are 530 with a capacity of three hundred beds or more. (Also, 316 of the 563 mental hospitals, 73 of the 449 tuberculosis hospitals and 34 of the 755 "other hospitals" have a capacity of three hundred beds or over.) Many of these institutions serve not only as community hospitals but as primary or secondary teaching hospitals for medical schools. Each is a vital unit in the country's scheme of medical care, and most of them will see a continuing growth in bed capacity and in scope and usefulness of service.

In the more distant past, persons of varying talents have been elected to administer hospitals. Outstanding success has attended the administration of hospitals not only by physicians but by men and women of other backgrounds—business administration, sociology, nursing, engineering and a host of others. Therefore physicians should not take it for granted that the medical practitioner has a "corner" on the administration of the larger hospitals. But he does possess an important advantage in his medical background, and if he acquires ability in the administrative field he has distinct talents over those of the man who cannot match his professional training.

Formerly engagement in hospital administrative work was, nine times in ten, the result of a drifting process whereby persons not specifically prepared for this work were induced by hospital boards or other agencies to undertake these complicated jobs. A number of hospitals committed the error of believing that because a man had a medical education he could successfully pilot the hospital, an admittedly medical institution. There were signal successes, but there were also many failures, in which the administrators lacked both education and natural ability for the work.

It is extremely probable that few physicians who are planning their careers are aware of recent developments whereby specialized university education is offered to the would-be hospital administrator. The University of Chicago was an early pioneer in this field. Strong impetus resulted, more recently, through the constructive interest of the W. K. Kellogg Foundation in encouraging leading universities to develop sound courses for teaching hospital administration at the graduate level.

The course at Columbia University was established in its School of Public Health in the fall of 1945 and is undergoing sound development. In 1946 the University of Minnesota and Washington University, St. Louis, established graduate courses in this field. Yale University, through its School of Public Health, will open its course in the fall of 1947. These four courses are proceeding under subsidy of the Kellogg Foundation, and Northwestern University supports courses of a similar nature.

The work at Columbia utilizes the facilities of the School of Public Health for courses in that science which are necessary to the background of these students and beamed to their needs. A faculty of full time and part time instructors in hospital administration handles the core of the work.

Each of the universities mentioned accepts physicians and qualified laymen for this course. The latter must be college graduates. In addition to one full year of academic study each of the universities requires a calendar year of administrative internship under preceptorship of a hospital administrator and in a hospital, both of which have met the requirements of the particular university for imparting this practical instruction. At the completion of internship Columbia University awards the Master of Science degree; the other universities have somewhat similar arrangements.

This article has a dual purpose. Hospital administration is a field of real opportunity for the physician, and as a physician-administrator I believe that the future development of the best in hospital administration and in organized medical care requires the talents of more physicians who are willing to undertake the necessary supplementary preparation for engaging in this work.

This discussion has been centered on hospital administration, but it would be an error not to call attention to the rapidly growing needs in the closely related fields of group clinic administration and nonprofit plans for hospital and medical insurance. Physicians seeking a career should take cognizance of the technics of present and future medical care administration in determining their own fields of usefulness.

The doctor who would explore the posibilities discussed herein should not lightly decide to follow this sort of work. He should have convinced himself that he will enjoy administrative work and that he will be content to apply his medicine on a broad but less personal basis than in the diagnosis, treatment and care of the illnesses of the individual. He will use his medical knowledge hourly, but he must realize that it would be suicidal to his success should he plan an administrative career in combination with the active practice of clinical medicine. He must enjoy the prospect of aiding, coordinating and potently influencing medical practice without placing himself in clinical competition with the doctors whom he aspires to serve.

SUMMARY

1. Hospital and related forms of medical administration offer fertile fields of opportunity for the physician.

2. Graduate education is now offered by representative universities to the physician interested in this type of work.

3. Medical administrative work offers opportunity for outstanding social usefulness and adequate tangible rewards to justify its consideration.

Director, St. Luke's Hospital; Professor of Hospital Administration, Columbia University.

1. Hospitals Registered by the American Medical Association, J. A. M. A. **130**: 1091 (April 20) 1946.

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Dental Practice Acts: Interpretation of Restrictions on Advertising.—The state board of dental examiners filed a petition to restrain the defendant dentist from engaging in certain advertising alleged to be a violation of the Texas penal code. From a judgment denying the prayer of the petition, the board of dental examiners appealed to the court of civil appeals of Texas.

Article 752 b, penal code, provides: "It shall be unlawful for any person, firm, or corporation to engage in or be guilty of any unprofessional conduct in the practice of dentistry, directly or indirectly. Any 'unprofessional conduct,' as used herein, means and includes any one or more of the following acts, to wit: . . . (*o*) advertising by means of large display signs, or glaring light signs, electric or neon, . . . directing the attention of the public to any such person or persons engaged in the practice of dentistry."

The defendant was a duly licensed and practicing dentist in the city of Dallas, Texas. During 1946 there appeared in the newspapers in the city of Dallas advertisements in size of approximately 4 by 4 inches, displaying Dr. Bickham's picture with his name underneath, and printed matter in type varying in size, the largest being approximately 1½ inches, reading: "How old are your plates And are they made out of the old-fashioned, hard-to-clean, unsightly gum materials? Get new, modern plates Which your dentist will construct with the new, light-absorbing, transparent teeth and lifelike gum materials and taken together, these materials when in the hands of a modern dentist, enable him to produce dentures that are both beautiful and hard to detect. Note—To present plate wearers: You may have your old teeth set in the new, beautiful gum materials. Out-of-Town Patients given special consideration. Crowns Bridges Extractions Fillings Dental X-Ray Office Hours: Weekdays Open 9 A. M. Dr. W. H. Bickham, Dentist. 1716½ Live Oak St. Phone R 2016." If such display advertisements come under the condemnation of Article 752 b, section (*o*), evidently a temporary injunction on such showing should have issued pending trial for permanency of such relief. The paramount issue, said the court, to be determined in construing this article (Art. 752 b, sec. (*o*)) is: What did the legislature mean by "large display signs" and are they prohibited thereby?

The Texas code, relating to interpretation and construction of words used in the penal code thereof, provides in Article 8: ". . . all words used in this Code, except where a word, term or phrase is specially defined, are to be taken and construed in the sense in which they are understood in common language, . . ." The words "large display signs" of the penal code must be given the "plain import" of the term and be interpreted in the "sense in which they are understood in common language," said the court. The definition of the word "sign" in Webster's New International Dictionary is: "A lettered board, or other conspicuous notice, placed on or before a building, room, shop or office to advertise the business there transacted, or the name of the person or firm conducting it; a publicly displayed token or notice." Another definition of the word "sign" is that in New Century Dictionary, which reads: "Now, usually, an inscribed board, plate, space, or the like serving for information, guidance, advertisement, etc., as on or before a building or a place of business, or along a street or road." Thus giving effect to the rules of construction and the definitions of the word "sign," said the court of appeals, we believe that the "usual sense" of the word, as used in "common language," and the "ordinary significance of the word," excludes the idea that "display ads" in newspapers is comprehended in the term "display signs." It seems clear, although abhorrent to the evident intent and purpose of the act, that a dentist may advertise in newspapers, by large display "ads" which are prohibited by means of "large display signs." Courts cannot extend subdivision (*o*), which forbids advertising by means of "large display signs," to newspaper advertisements. "Signs" are not "ads." The statute having limited the manner and place of advertising by "signs," without extending the extent and manner of such advertisement to include newspapers, the judgment of the court below was held correct in denying the injunction, and the judgment in favor of the defendant dentist was affirmed.—*State Board of Dental Examiners v. Bickham, 203 S. W. (2d) 563 (Texas, 1947).*

Malpractice: Osteopathic Manipulation of Fracture Joint.—The plaintiff sued for damages alleged to have resulted from the malpractice of the defendant osteopath. The defendant obtained a judgment of nonsuit in the trial court, so the plaintiff appealed to the Supreme Court of California.

On January 4 the plaintiff sustained a fracture of the humerus, and received immediate treatment from the defendant osteopath, in whose office she was employed After taking an x-ray, he placed her arm in a plaster cast with the forearm in a horizontal position. Infra-red light treatments were administered until January 31, when the cast was cut and further x-ray pictures were taken. On February 3, according to the plaintiff's testimony, the defendant massaged her arm and flexed her elbow about in "all directions" for about ten minutes, and the manipulation caused very definite pain. On February 5 he gave the same manipulative treatment, except that it was more vigorous. The plaintiff said that the defendant massaged her arm and flexed her elbow every few days thereafter, and each of the subsequent treatments was "more violent and longer." During the March 3 or 4 treatment the plaintiff screamed with pain, but the defendant did not stop. On March 14 the defendant, with the assistance of another doctor, gave the plaintiff an anesthetic and extended and straightened her arm to the full 180 degree angle. A few days later he swung her arm while she was holding a weight, and the pain was so intense she "couldn't stand it." On March 24 she again returned to his office and "screamed" from pain when her right hand was extended above her head. Following this last treatment the plaintiff secured another doctor.

The defendant testified that he did not give the first manipulative treatment until six weeks after the arm was fractured. When asked whether he had continued to manipulate the plaintiff's elbow after she complained of pain, he replied: "No, I do not manipulate the joint of that kind. We use what is known as the manipulation to tolerance, and that is the point at which the patient begins to complain." He stated that if the manipulation was carried beyond that point "there would be danger of doing injury to the bone which had been fractured." He was then asked: ". . . is it necessary, then, in treatment of a fracture of this type to be very careful about the manipulation of the joint beyond tolerance?" and replied, "That is correct." To the question, "In addition to being brutal, that would be bad practice, wouldn't it?" he answered "Yes."

In passing on the propriety of a judgment of nonsuit, said the Supreme Court, every favorable inference and presumption fairly arising from the evidence and tending to sustain the plaintiff's case must be accepted as true. When the plaintiff's evidence, the court continued, is considered in the light of these factors, it is apparent that she has established a prima facie case of negligence. A physician, said the court, is required to have the degree of learning and skill possessed by physicians of good standing practicing in the same locality. Although the defendant did not expressly refer to the practice followed by other doctors in the community, he did testify as to what was proper practice, and it is reasonable to infer that his testimony was based on the standard of care used by physicians in the locality. If he failed to conform to the proper practice as set forth in his own testimony, he did not act as a reasonable physician should under the circumstances. The evidence would have supported findings that the first manipulative treatment was given on February 3, about four weeks after the fracture, that four others were given within six weeks of the accident and that, despite the plaintiff's protests and repeated declarations of pain, the manipulation was carried beyond the point of tolerance. The Supreme Court therefore concluded that a jury could have found that the defendant was negligent in departing from the standard of care required. The judgment of nonsuit in favor of the defendant was accordingly reversed.—*McCurdy v. Hatfield, 183 P. (2d) 269 (Calif., 1947).*

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1937 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied with stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted.

Alabama State Medical Assn. Journal, Montgomery

17:93-124 (Sept.) 1947

Surgical Management of Gastric and Duodenal Ulcers. O. T. Clagett.—p. 93.
Fallacy of Conjoined Tendon: Etiology and Repair of Inguinal Hernia. S. A. Zieman.—p. 98.
Workable Concept for Treatment of Toxic Thyroid. E. A. Henderson.—p. 101.
Present Day Trends in Anesthesiology. E. B. Robinson.—p. 105.

17:125-152 (Oct.) 1947

Arrhenoblastoma: Case Report. J. P. Hardy and A. F. Toole.—p. 125.
Importance of Follow-Up Roentgenograms in Pulmonary Disease. C. A. Good.—p. 129.
Clinical Application of Sex Hormones in Gynecology. H. H. Thomas.—p. 134.
*Experiences With Brush's Method for the Initial Stabilization of Diabetic Children. B. P. Clark.—p. 137.

Brush's Method for Diabetic Children.—According to Clark it is becoming well recognized that diabetes in children and in adults represents two different diseases and that there is a uniform response of children with diabetes mellitus to the treatment of their initial episode of glycosuria. Brush developed a method for the uniform standardized treatment of the initial episode of hyperglycemia. The entire need of the child for insulin is supplied, initially, by the exogenous route. Brush has supplied tables for the calculation of the daily dose of insulin, the number of calories and the amount of carbohydrates, fats and protein in the diet. The tables should be followed strictly. The high initial dose of insulin is divided into four daily doses, one to be given fifteen minutes before each meal and a smaller one at four in the morning. The chief sign of the beginning recovery of the islet system is insulin shock. This can usually be expected between the sixth and the tenth day of treatment and is easily controlled by the administration of sweetened orange juice. Now the dosage of insulin is reduced daily according to the schedule given by Brush until the minimum level is reached. This is usually between 3 and 9 units per day. Clark describes some experiences with Brush's method for the initial stabilization of the diabetic child and shows that it has several advantages over other methods.

American Heart Journal, St. Louis

34:311-470 (Sept.) 1947

Physiologic Changes in Circulation During and After Obstetric Labor. Ellen Brown, J. J. Sampson, E. O. Wheeler and others.—p. 311.
*Voluntary Acceleration of Heart in Subject Showing Wolff-Parkinson-White Syndrome: Clinical, Physiologic and Pharmacologic Studies. H. Feil, H. D. Green and D. Eiber.—p. 334.
*Subacute Bacterial Endocarditis of Undetermined Etiology. L. Loewe and H. B. Eiber.—p. 349.
Auricular Fibrillation with Aberration Simulating Ventricular Paroxysmal Tachycardia. J. L. Gouaux and R. Ashman.—p. 366.
Supernormal Phase of Recovery of Conduction in Human Heart. I. Mack, R. Langendorf and L. N. Katz.—p. 374.
*Electrocardiogram in Neurocirculatory Asthenia, Anxiety Neurosis, or Effort Syndrome. P. D. White, M. E. Cohen and W. P. Chapman.—p. 390.
Relations of T_1 and T_3. E. Goldberger.—p. 395.
Circulatory Effects of Three Modifications of Valsalva Experiment: An Experimental Survey. R. F. Rushmer.—p. 399.

Voluntary Acceleration of Heart.—Voluntary acceleration of the heart has been reported in 20 cases. Feil and his associates describe a new case. The patient was a medical student, aged 23, who tried to dilate his pupils voluntarily by using the fear response. He observed that the dilation of his pupils was accompanied by tachycardia. After repeated experiences he was able to dissociate the effort to dilate his pupils and to concentrate on the will to accelerate his heart. A pertinent fact was the occurrence of attacks of paroxysmal tachycardia five or six times a year, lasting two or three hours. These attacks started and stopped suddenly and were unrelated to any effort at voluntary acceleration. One such attack was observed by one of the authors. It was stopped by right carotid sinus pressure. The patient's electrocardiogram was typical of the Wolff-Parkinson-White syndrome (short PR interval and prolonged QRS complex). Epinephrine and atropine given in physiologic doses did not prevent the ability of the subject to control his heart action. Epinephrine appeared to have an augmenting effect on acceleration. Drugs increasing vagus tone (digitalis, quinidine and ergotamine tartrate) did not prevent the acceleration and deceleration. No physical means of acceleration (changes in respiration or muscular activity) were demonstrated. The electroencephalogram demonstrated that psychic activity preceded the acceleration. The diminution in the peripheral blood flow and the dilation of the pupils further substantiate the importance of the impulses via the sympathetic system. The ability of the subject to influence his heart rate was chiefly through sympathetic control, but inhibition and augmentation of vagus influence also played a part.

Subacute Bacterial Endocarditis of Undetermined Etiology.—Loewe and Eiber encountered in a series of 166 patients with subacute bacterial endocarditis, 11 with consistently sterile blood cultures despite recourse to anaerobic methods, enriched mediums, arterial punctures and cultures taken after administration of epinephrine. Ten of the 11 patients were successfully treated. Nine of these 10 responded to combined penicillin and heparin therapy. In the tenth patient the infection was terminated by streptomycin, after the combination of penicillin and heparin had failed to accomplish this. Two of the patients who were successfully treated subsequently succumbed to intractable heart failure. In one of these necropsy revealed valves so mutilated as to be incompatible with life. No bacteria could be recovered from the healed valves, nor could organisms be seen in histopathologic sections. In the other patient who succumbed, necropsy disclosed the typical pathologic picture of active subacute bacterial endocarditis. Organisms could not be recovered from the thromboulcerative endocardial lesions, although organisms were observed in histopathologic preparations. Observations on these 11 cases indicate that such patients should be treated as promptly and intensively as though they had positive blood cultures.

Electrocardiogram in Neurocirculatory Asthenia.—White and his associates summarize data secured in the analysis of electrocardiograms of 50 soldiers with neurocirculatory asthenia and 50 civilian men and women with anxiety neurosis and neurocirculatory asthenia. They failed to find a characteristic pattern. The few variations from the average normal record are those usually encountered in a group of healthy young men, and either are associated with well-known factors such as body build, pulse rate and posture or are the effect of past illness.

American Journal of Clinical Pathology, Baltimore

17:671-760 (Sept.) 1947

Gargoylism: Review of Literature and Report of Sixth Autopsied Case with Chemical Studies. R. Straus, R. Merliss and R. Reiser.—p. 671.
Prozone Phenomenon in Rh Blocking Serums. P. G. Hattersley and Margarette L. Fawcett.—p. 695.
Significance of Accelerated Reaction in Determination of Prothrombin Time of Diluted Plasma. H. S. Tuft and R. E. Rosenfield.—p. 704.
Variations in Prothrombin and Antithrombin in Patients with Thrombosing Tendencies. Margaret Hurn, N. W. Barker and Frank D. Mann.—p. 709.
Variations in Prothrombin and Antithrombin Following Administration of Dicumarol. Margaret Hurn, N. W. Barker and F. D. Mann.—p. 712.
*Anthrax Meningitis: Report of Case of Internal Anthrax with Recovery. R. H. Shanahan, J. R. Griffin and A. P. von Auersperg.—p. 719.
Deaths Following Use of Abortifacient Paste: Report of 2 Cases. W. Kulka.—p. 723.

Anthrax Meningitis.—Shanahan and associates report the case of a man, aged 57, who was employed as a wool picker at a carpet shop for two weeks. He appeared for examination with a vesicular lesion on the upper lip. Anthrax was suspected

and the patient was hospitalized. The initial treatment consisted of 100,000 units of penicillin followed by 100 cc. of antianthrax serum, both given intramuscularly. On the second day the temperature rose to 102 F. During the night the patient began a twitching in the arms and face; he complained of pain in the back of the neck. Cultures of blood and pus were positive for Bacillus anthracis. Since meningeal involvement was suspected, penicillin was administered intrathecally. There was excellent response to the medication, which consisted of penicillin given intramuscularly, intrathecally and locally, antianthrax serum given intramuscularly and sulfadiazine by mouth. Owing to the rapid development of meningeal involvement in anthrax infection, it appears that antianthrax serum alone is ineffective. Inasmuch as previous cases of anthrax meningitis treated without penicillin all terminated fatally, one may speculate on a synergistic action between the antianthrax serum and penicillin in this case. Anthrax infection among wool workers is sufficiently frequent that one should consider cutaneous lesions in such workers suggestive. The incidence of meningeal involvement in anthrax infection is about 5 per cent.

American Journal of Diseases of Children, Chicago

74:265-390 (Sept.) 1947

Prevalence of Dental Caries in Malnourished Children: Clinical Study. S. Dreizen, A. W. Mann, T. D. Spies and Thelma A. Skinner.—p. 265.
*Determination of Anti-Rh Antibody in Infants with Erythroblastosis Fetalis. W. E. Wheeler and Mary Louise L. Scholl.—p. 274.
*Chemical Studies in Children with Nephrotic Syndrome. S. P. Gottfried, J. F. Steinman and B. Kramer.—p. 283.
Porphyria and Porphyrinuria: Report of a Case; Review of Porphyrin Metabolism with a Study of Congenital Porphyria. I. Dunsky, S. Freeman and S. Gibson.—p. 305.
Hyperimmune Serums in Treatment of Whooping Cough: Clinical Results, with Notes on Bacteriologic Studies and Cutaneous Tests. J. L. Kohn and others.—p. 321.
*Acetylsalicylic Acid Poisoning with Recovery. J. B. Gillespie and R. E. Dukes.—p. 334.

Anti-Rh Antibody in Erythroblastosis Fetalis.—Wheeler and Scholl think that since erythroblastosis fetalis is caused by the combination of maternal anti-Rh antibody with Rh antigen contained in fetal tissue, its immunologic diagnosis should rest on the demonstration of such an antigen-antibody combination in the fetus. There are two types of maternal antibody, the complete and the incomplete. A method which liberates the anti-Rh antibody by heat from its combination with the red cells of the erythroblastotic baby will demonstrate both the complete and incomplete type of antibody. The authors also describe observations with the method that demonstrates red cells sensitized with anti-Rh antibody in the blood of babies with erythroblastosis by the use of appropriately absorbed anti-human-serum. The use of these methods for verifying the diagnosis of erythroblastosis in the baby's blood is emphasized. The significance of the reversibility of the antigen-antibody reaction, and the possibility that a damaging antigen-antibody reaction might exist in tissues other than blood cells, is discussed in relation to the pathogenesis of erythroblastosis. The authors observed 20 infants with erythroblastosis. Anti-Rh antibody was liberated according to the described method in 19 of the 20 cases. In 1 case the baby was not observed until the ninth day, when the hemolytic process had apparently run its course.

Blood Chemistry in Nephrosis.—Gottfried and his collaborators report observations on the blood chemistry, the clinical course and the therapeutic results obtained in 10 children with the nephrotic syndrome. Levels of amino acid nitrogen in the plasma were normal or slightly elevated, even during periods of so-called nephrotic crises. Dextrose tolerance curves suggested some disturbance in the absorption and utilization of carbohydrates in nephrotic patients. Carotene values were considerably elevated, in keeping with the lipemia. Vitamin A levels, however, were normal or only slightly elevated. Hepatomegaly was frequent in these children. All patients manifested one or more signs of impaired hepatic function, but the departures from normal were relatively slight. The trend of formation or resorption of edema varied inversely with the serum protein levels when the total serum proteins exceeded 4 Gm. or the serum albumin exceeded 1.5 Gm., per hundred cubic centimeters. Below these levels edema tended to increase progressively, regardless of fluctuations in the concentration of protein in the serum. This suggests that other factors than colloid osmotic pressure are primarily operative in determining the course of the edema in this low protein range. The most useful therapeutic measures appear to be restriction of salt, parenteral replacement of proteins and control of infection. Penicillin seemed the chief factor in reducing the fatality rate. The evidence regarding the benefits to be obtained from thyroid, diuretics and hydragogue cathartics is less convincing. Protein hydrolysates and synthetic amino acid mixtures, as well as the various lipotropic agents, may eventually prove to be of value.

Acetylsalicylic Acid Poisoning.—Gillespie and Dukes report 2 cases of acetylsalicylic acid poisoning in young children. Both were boys three years of age. They had been found eating 5 grain (0.32 Gm.) acetylsalicylic acid tablets, and it was estimated that they had ingested about fifteen such tablets. The most prominent symptom in the clinical picture was hyperventilation. Despite the fact that the degree of acidosis, as indicated by the carbon dioxide combining power of the blood, was greater in case 2, the patient was less hyperpneic and never appeared as seriously ill as the first child. Cyanosis was not noted in either of the children. The first patient passed through a period of irritability and delirium, during which death appeared imminent. From twelve to twenty-four hours had elapsed between the ingestion of the acetylsalicylic acid and the development of the intoxication. Both children responded promptly to the intravenous administration of a solution of sodium bicarbonate. The hyperpnea diminished almost immediately after the infusion of this solution. Decrease of the acidosis, as judged by the carbon dioxide combining power of the blood and the disappearance of ketone bodies from the urine, was also noted shortly after the intravenous sodium bicarbonate therapy.

American Journal of Hygiene, Baltimore

46:149-295 (Sept.) 1947

*Epidemiology of Acute Respiratory Infections Conditioned by Sulfonamides: VIII. Effect of Sulfadiazine on Nasopharyngeal Carriers of Hemophilus Influenzae, H. Hemolyticus and Neisseria. M. Siegel.—p. 149.
Contact Typhoid Fever in a State Mental Hospital: Report of an Epidemiologic and Laboratory Investigation. M. Dorothy Beck, Lucy E. French, Esther Allen and M. H. Merrill.—p. 162.
Elimination of Viable Bacteria from Cultures of Endamoeba Histolytica and Subsequent Maintenance of Such Cultures. L. Jacobs.—p. 172.
Exposed Dental Pulp as a Portal of Entry for Virus of Poliomyelitis. S. Finn, R. F. Korns and Anne M. Bahlke.—p. 177.
*Outbreak of Q Fever in Chicago Packing House. C. C. Shepard.—p. 185.
Blood Levels and Excretion Rates of Antimony in Persons Receiving Trivalent and Pentavalent Antimonials. G. F. Otto, T. H. Maren and H. W. Brown.—p. 193.
Periodic or Cyclically Recurring Phenomena of Vivax Malaria Infections. P. Putnam, M. F. Boyd and Pauline A. Mead.—p. 212.
Rapid Infection of a Family After Introduction of Poliomyelitis Virus. A. R. Zitek.—p. 248.
In Vitro Study of Mechanism Producing Rapid Diminution in Parasitemia in Ducks Infected with Plasmodium Lophurae. R. H. Rigdon.—p. 254.
Studies on Syphilis in Eastern Health District of Baltimore City: IV. Syphilis Among Parturient Women as an Index of Trend of Syphilis in Community. G. M. Leiby, T. B. Turner, E. G. Clark, R. Dyar and F. C. Kluth.—p. 260.
Observations on Tsutsugamushi Disease (Scrub Typhus) in Assam and Burma: Recovery of Strains of Rickettsia Orientalis. G. E. Davis, R. C. Austrian and E. J. Bell.—p. 269.
Cross Immunity in Experimental Syphilis, Yaws and Venereal Spirochetosis of Rabbits. T. B. Turner, Charlotte McLeod and Elaine L. Updyke.—p. 287.

Effect of Sulfadiazine on Nasopharyngeal Carriers.—In a preliminary bacteriologic survey of 272 feeble-minded children Siegel found that all were carriers of Hemophilus influenzae and Neisseria, and at least 71 per cent harbored Hemophilus hemolyticus in the nasopharynx. Sixty children with heavily positive cultures were chosen for the study. The blood levels varied with the dosage and the subject. The average values for daily dosages of 0.5, 1 and 2 Gm. were 1.7, 2.8 and 6.6 mg. per hundred cubic centimeters, respectively. In 2 children the administration of sulfadiazine had to be discontinued on the thirteenth and fifty-first days, respectively, on account of generalized rash and drug fever. The throat flora was studied with the aid of a differential agar medium containing 0.1 unit of penicillin per cubic centimeter. The resistance

of the organisms in vivo varied, H. hemolyticus being uniformly sensitive, H. influenzae less sensitive and Neisseria quite resistant. Following the use of sulfadiazine there was evidence of an increase in drug tolerance of H. influenzae and of a selective decrease in the frequency of sensitive strains, which was reversible after withdrawal of therapy.

Q Fever in a Chicago Packing House.—Shepard says that although the causative organism of Q Fever, Rickettsia burneti, has been isolated from ticks in several parts of the United States, only one naturally occurring case was reported in this country in 1941, before the outbreak in Amarillo, Texas, in March 1946. In August 1946 an outbreak of Q fever took place in men working on a sheep and calf killing and dressing floor of one of the large packing houses in Chicago. Among the 81 men employed on this floor, 33 cases of Q fever were found chiefly by means of the complement fixation test. Splattering of blood and other body fluids was particularly noticeable in such operations as the washing of carcasses and the handling of viscera. Among the 19 men studied who worked at these jobs there were 15 cases. The average incubation period was estimated to be nineteen to twenty-five days.

American Journal of Public Health, New York

37:1247-1370 (Oct.) 1947. **Partial Index**

A Future for Industrial Medicine. L. J. Goldwater.—p. 1247.
Uses of Statistical Data in State Health Departments. Ellen B. Whiteman.—p. 1267.
Statistics in Planning and Evaluation of Health Procedures. H. Muench.—p. 1273.
Discussion of Bacteriologic Standards for Dehydrated Foods. H. E. Goresline.—p. 1277.
Problem of Reconstituted Milk. G. H. Hauser and W. H. King.—p. 1284.
Safe and Beneficial Utilization of Nuclear Energy. A. H. Dowdy.—p. 1291.
American Academy of Pediatrics Study of Child Health Services: Results to Date. Katherine Bain, J. P. Hubbard and C. L. Williams Jr.—p. 1297.
*Value of Industrial Hygiene. T. L. Hazlett.—p. 1302.
Age and Sex Variations in Hospital Utilization. (Example of Morbidity Data Available from Blue Cross Records.) J. D. Colman.—p. 1307.
People Win for Public Health in Colorado. Florence R. Sabin.—p. 1311.
Standards of Dental Care in Public Health Programs for Children. N. F. Gerrie.—p. 1317.
Method for Assessing Sanitizing Efficiency of Quaternary Ammonium and Hypochlorite Products. C. K. Johns.—p. 1322.
*Congenital Defects in Year of Epidemic Rubella. R. E. Ober, R. J. M. Horton and R. F. Feemster.—p 1328.

Value of Industrial Hygiene.—Hazlett says that of the working population of 60,000,000 in the United States there are probably 15,000,000 persons working in industries which use potentially hazardous materials or processes. About one third of these are exposed to a material or process which may involve a potential health hazard. The value of industrial hygiene is being demonstrated by the preservation of the health of these persons. One of the outstanding accomplishments in the field of control of occupational diseases during the war period was done in government-owned ordnance explosive plants. Among 309,000 operating employees in one hundred and one plants there were only 28 fatalities because of occupational disease. Twenty-two of these were caused by trinitrotoluene (TNT), whereas during the relatively limited production of this explosive during World War I it caused 475 fatalities. Many industrial organizations have equally commendable records. The successful utilization of atomic energy will depend on the elimination of health hazards associated with the variety of radiations which occur in their use. The author cites studies on possible dangers in the manufacture of insecticides and radar equipment. The impetus given to the study and control of industrial health hazards during the past few years has resulted in a fuller appreciation of the value of industrial hygiene.

Congenital Defects in a Year of Epidemic Rubella.—Ober and his associates report a survey made in Massachusetts to detect anomalies in infants resulting from maternal rubella. The year 1943 was selected for such a study for several reasons: Nearly 35,000 cases of rubella had been reported during that year, nearly twice the usual incidence; it was recent enough for individual memories to recall important facts; the children would be old enough for the anomalies to have been recognized. Among 54 pregnancies reported in replies to questionnaires sent to women of child-bearing age, 8 resulted in infants with abnormalities and 9 ended in abortions or stillbirths. Eleven of these 17 abnormal pregnancies were in women who contracted rubella during the first trimester. Of 9 pregnancies reported by physician in response to questionnaires, only 3 produced normal infants. Eight of the 9 women contracted rubella in the first trimester. The authors admit, however, that caution is necessary in attributing all such defects in infants to maternal rubella. They stress the need of more comprehensive surveys to determine the comparative incidence of abnormal pregnancies in other virus and bacterial diseases as well as abnormalities in pregnancies not complicated by communicable diseases.

American Journal of Tropical Medicine, Baltimore

27:527-661 (Sept.) 1947

*Oral Emetine in Treatment of Intestinal Amebiasis. B. C. Shrapnel.—p. 527.
Alcoholic Extract Medium for Diagnosis and Cultivation of Endamoeba Histolytica. E. C. Nelson.—p. 545.
Metabolism of Chiniofon Using Radioactive Iodine. E. C. Albright, D. L. Tabern and E. S. Gordon.—p. 553.
Types of American Cutaneous Leishmaniasis, Dermatological Aspects: Review. L. Goldman.—p. 561.
Characteristics of Foreign Vivax Malaria Induced in Neurosyphilitic Patients. M. D. Young, J. M. Ellis and T. H. Stubbs.—p. 585.
Molluscan Intermediate Host and Schistosomiasis Japonica: III. Experimental Infection of Oncomelania Quadrasi, Molluscan Intermediate Host of Schistosoma Japonicum. G. W. Hunter, H. J. Bennett, J. W. Ingalls Jr. and E. Greene.—p. 597.
Rectoscopic Biopsy by Transparency: New Diagnostic Method for Schistosoma Mansoni. C. Ottolina.—p. 603.
Filarial Infection in Costa Rica. D. C. A. Butts.—p. 607.
Reactions of Natives of Okinawa and of American Personnel to Skin Tests with Test Antigen Prepared from Microfilariae of Dirofilaria Immitis. M. B. Franks, B. M. Chenoweth Jr. and N. R. Stoll.—p. 617.
*Evaluation of Penicillin in Treatment of Yaws: Final Report. J. H. Dwinelle, A. J. Sheldon, C. R. Rein and T. H. Sternberg.—p. 633.
Salmonella Infections in Panama: Review of 219 Consecutive Hospital Cases Occurring in Five Year Period 1942-1946. L. L. Henderson.—p. 643.
Carrion's Disease: Study of Incubation Period in 13 Cases. W. E. Ricketts.—p. 657.

Oral Emetine in Intestinal Amebiasis.—Shrapnel reviews observations on 25 adults and 5 children with acute and chronic forms of intestinal amebiasis who were treated by the oral administration of enteric-sealed tablets of emetine hydrochloride. Adults were given 2 grains (0.13 Gm.) daily for twelve days, and the children 1 grain (0.06 Gm.) daily for twelve days. Nausea, vomiting or other toxic symptoms were not manifested. Nineteen of the adults and all 5 children were restudied in from two to nine months following the original treatment. Clinical cure was obtained in all cases, but parasitologic cure failed in 1 adult, who was found to harbor Endamoeba histolytica trophozoites seven months after receiving the drug. Emetine hydrochloride in enteric-sealed tablets, administered orally, provides a concentration of emetine in the intestinal tract which closely approaches the amebicidal concentration necessary to eradicate the parasite without producing toxic side effects.

Penicillin in Treatment of Yaws.—Dwinelle and his associates report a follow-up on patients with yaws who were treated with penicillin either in aqueous solution or in oil with beeswax. Clinical and serologic observations were made on 446 of a total of 500 patients for varying lengths of time up to twelve months. Three hundred and twenty were followed for a period of ten to twelve months after treatment. Clinical response to treatment was uniformly excellent, but serologic response was not. Follow-up observations over a period of ten to twelve months after treatment are not sufficient to permit a comprehensive evaluation of the efficacy of penicillin in the treatment of yaws. It is not possible to make a strict comparison of the results of treatment of penicillin in aqueous solution with penicillin in oil with beeswax, because of the difference in treatment schedules employed. Penicillin is probably the drug of choice in the treatment of yaws. Penicillin in oil with beeswax is of considerable public health value in countries such as Haiti, where large numbers of patients must be treated on an ambulatory basis in rural clinics. Its use can be expected to successfully control cutaneous lesions and therefore prevent the spread of infection.

American Review of Tuberculosis, New York

56:175-266 (Sept.) 1947

Late Results of Thoracoplasty. R. Douglass.—p. 175.
Tuberculous Pleurisy with Effusion: An Analysis of 215 Cases Hospitalized at an Army Chest Center. I. G. Karron and R. K. Purves.—p. 184.
Chronic Empyema: Irrigation Treatment with Glycerite of Hydrogen Peroxide Solution; Preliminary Report. W. B. O'Brien, E. A. Brown and H. Pearse.—p. 190.
Nonreactors to Tuberculin: Analysis in a Large Sanatorium. M. R. Lichtenstein.—p. 198.
Tubercle Bacillus Antigens: Biological Properties of Two Substances Isolated from Paraffin Oil Extract of Dead Tubercle Bacilli. N. Choucroun.—p. 203.
*Streptomycin in Experimental Tuberculosis: I. Its Effect upon a Well-Established Progressive Tuberculous Infection in Guinea Pigs. W. Steenken Jr. and E. Wolinsky.—p. 227.
Reduction of Potassium Tellurite by Mycobacterium Tuberculosis. L. Sula.—p. 241.
Pulmonary Hematogenous Tuberculosis in the Adult: Anatomic Observations. D. M. Spain.—p. 249.

Streptomycin in Experimental Tuberculosis.—Steenken and Wolinsky injected 0.021 mg. of the human virulent strain H 37 R_v subcutaneously into 34 guinea pigs, of which 8 had previously been vaccinated with H 37 R_v and 26 were normal animals. Forty-nine days later, when the disease was well established, streptomycin therapy was started on 14 nonvaccinated and 4 vaccinated animals. Each treated pig was given 24,000 units (micrograms) per day subcutaneously in doses of 4,000 units every four hours for twenty days. The dosage was then reduced to 16,000 units per day. After forty days, half of the nonvaccinated animals and all 4 vaccinated animals were taken off treatment and allowed to live for another eighty-eight days, when those still surviving were killed. All the nonvaccinated controls died of tuberculosis within sixty-nine to a hundred and forty days. None of the treated pigs, and 1 of the vaccinated controls, died during the hundred and seventy-five days of the experiment. The animals treated continuously for a hundred and twenty-five days showed little tuberculous disease at necropsy. Virulent tubercle bacilli were recovered from 5 of these 7 pigs by subinoculation. The animals treated for forty days only demonstrated a slowly progressive, chronic type of tuberculosis at autopsy, similar to that of the vaccinated controls, and virulent tubercle bacilli were recovered from all 7 by subinoculation and subculture. Skin sensitivity to 5 per cent old tuberculin decreased consistently during streptomycin treatment. Streptomycin was apparently well tolerated by the guinea pigs.

Archives of Internal Medicine, Chicago

80:293-422 (Sept.) 1947

*Sarcoidosis: A Clinical and Roentgenologic Study of Twenty-Eight Proved Cases. J. J. McCort, R. H. Wood, J. B. Hamilton and D. E. Ehrlich.—p. 293.
*Penicillin in Cardiovascular Syphilis: Early Reactions to Administration. H. A. Tucker and T. W. Farmer.—p. 322.
Rheumatic Pneumonitis: Case of Widespread Chronic (Proliferative) Type with Acute (Exudative) Foci. E. E. Muirhead and A. E. Haley.—p. 328.
*Contagiousness of Coccidioidomycosis: Experimental Study. S. R. Rosenthal and J. B. Routien.—p. 343.
Osteogenesis Imperfecta: Study of Five Generations. C. S. Kellogg.—p. 358.
Neurologic Manifestations of Infectious Mononucleosis: with Special Reference to Guillain-Barré Syndrome. C. H. Peters, A. Widerman, A. Blumberg and W. A. Ricker Jr.—p. 366.
Analysis of a Four Year Epidemic of Mumps. A. Y. Eagles.—p. 374.
Allergic Lesions Following Thrombophlebitis. M. Naide.—p. 388.
Hepatic Cirrhosis and Testicular Atrophy. L. J. Rather.—p. 397.
Incidence of Tuberculosis Pulmonary Cavities in Unexpected Deaths Investigated at Necropsy. E. M. Medlar.—p. 403.

Sarcoidosis.—Summarizing their observations on 28 patients with sarcoidosis who were sent to a military hospital that functioned as a center for the treatment of tumors, McCort and his co-workers say that all their patients had intrathoracic lymphadenopathy and that all except 2 had enlargement of the superficial lymph nodes. Roentgen study of the 28 patients revealed enlargement of the paratracheal lymph nodes in all; enlargement of the peribronchial lymph nodes in 25; pulmonary parenchymal involvement in 15; pleural effusion in 2; pericardial effusion in 1, and osseous changes in the hands of 6. In 11 of the 28 cases the enlargement of the intrathoracic lymph nodes was more prominent on the right side, which may be explained on the basis of the anatomic observation that in the normal chest the lymph nodes are more numerous on this side. This fact is without value in the differential diagnosis of benign and malignant lymphogranuloma, contrary to what was once suspected. In 27 of the 28 cases the enlarged intrathoracic lymph nodes tended to remain discrete and well defined. There was but 1 death in this series, which was due to failure of the right side of the heart secondary to extensive infiltration of the lungs. Radiation therapy was not of value in the treatment of the enlarged lymph nodes of sarcoidosis in the 2 cases in which it was tried. The authors were unable to confirm the incidence of leukopenia observed by others. Anemia was found in only 2 cases. Eosinophilia was infrequent, and the monocytes were not consistently increased. No instance of a false positive reaction to a serologic test for syphilis was noted. The finding of a frequently negative reaction to the tuberculin test and of a high globulin value was confirmed.

Penicillin in Cardiovascular Syphilis.—Tucker and Farmer treated 28 patients with syphilitic aortic insufficiency and 8 with thoracic aortic aneurysm by the intramuscular route with sodium penicillin in aqueous solution in total dosages ranging from 2,000,000 to 15,000,000 Oxford units. Five patients had fever within the first sixteen hours of treatment.. Two patients with long-standing angina at rest had attacks of usual severity and frequency during and subsequent to administration of penicillin. In no instance was the treatment schedule interrupted. Significant differences in the incidence of febrile reactions or cardiovascular symptoms did not occur in 9 patients receiving small initial doses (500 to 3,000 Oxford units) as compared with 21 patients given large initial doses (25,000 to 100,000 Oxford units) of penicillin. The authors conclude that the absence of reported severe reactions tends to confirm their impression that the dangers of severe untoward reactions may have been unduly emphasized. More work must be done with various dosages of penicillin in patients with cardiovascular syphilis before final conclusions are justified.

Contagiousness of Coccidioidomycosis.—Rosenthal and Routien consider the contagiousness of coccidioidomycosis, because with the high incidence of infection that occurred in large numbers of troops trained in such endemic areas as Southern California, parts of Texas, Arizona and New Mexico and with subsequent demobilization, numerous soldiers harboring the fungus will return to all parts of the United States. Coccidioides immitis, the fungus responsible for the disease, has two distinct phases in its development. It is found in the animal host as a refractile thick-walled spherule filled with spores. The spores may be liberated by rupture of the cyst, whereupon each spore may develop into a spherule. This cycle is continuous or limited in vivo, depending on the progression of the disease. In culture the fungus produces mycelial threads and spores (chlamydospores); the latter are cylindric and thus differ from the spheres. The investigations made by the authors have been directed into two channels: (*a*) the determination of whether the spherule outside of the body can remain viable for a long time without the production of mycelial threads or spores and (*b*) the determination of whether sputum, pus or exudate from human sources containing spherules can produce infection in guinea pigs on instillation into the respiratory tract. The spherules of C. immitis remain viable under certain conditions and do not produce hyphae and chlamydospores in exudates from human sources for at least one hundred and ten days (experiments still in progress). By instilling spherule-containing sputum or exudates from human or animal sources into the bronchi of guinea pigs and propelling them by air pressure into the finer ramifications of the bronchioles and alveoli, it is possible to produce coccidioidomycosis in 100 per cent of the animals. The lesions are localized for the most part in the upper portions of the lungs, are single or multiple, have a lymph node component and are not generalized, thus simulating the human infection. These experiments show that spherules (or sporangia) can be infective through the respiratory route from man to animal and from animal to animal. It is concluded that active primary or progressive coccidioidomycosis in human beings should be considered contagious until proved otherwise.

Archives of Pathology, Chicago

44:207-324 (Sept.) 1947

*Multiple Myeloma: Survey Based on 35 Cases, 18 of Which Came to Autopsy. L. Lichtenstein and H. L. Jaffe.—p. 207.
*Mechanism of Lipophage Deposition in Atherosclerosis. I. Gordon. —p. 247.
Distribution of Parietal Cells in Gastric Disease. W. A. Meissner. —p. 261.
Factors Influencing Brown Degeneration of Adrenal Gland in Swiss Albino Mouse. C. E. Tobin and Jean P. Birnbaum.—p. 269.
Heterotopic Blood Formation in Experimental Cholesterol Arteriosclerosis. R. Altschul.—p. 282.
Toxicity of "Stilbamidine": Study of Effects of Chronic Intoxication. L. D. Seager and Gina Castelnuovo.—p. 287.
Hair Growth in Skin of Guinea Pigs Painted with 20-Methylcholanthrene. M. Silberberg and Ruth Silberberg.—p. 297.
Ultraspectrophotometric Studies of Extracts of Normal and of Tumor Tissue of Human Origin. Mona Spiegel-Adolf and M. E. Sano. —p. 307.

Multiple Myeloma.—Lichtenstein and Jaffe report 35 cases of multiple myeloma, in 18 of which necropsies were made. Twenty-six of the patients were between 40 and 60 years of age, though some were in their 30s, and one patient was only 13 years of age when the first manifestations of the disease appeared. Multiple myeloma may be slightly more prevalent in men than in women, but the statement that the condition is at least twice as frequent in men does not seem to be warranted. Multiple myeloma is a distinctive malignant disease of the skeleton primarily, which apparently takes its departure from the myeloid formative tissue proper. The skeletal progress of the disease may be steady and rapid, sometimes from the beginning and sometimes after a static period. In some cases the disease may flourish in one bone as a so-called solitary myeloma for months or even years. Extraskeletal tumor foci were encountered in 2 of the authors' patients who came to autopsy, in one instance in the liver and in the other in the spleen. In some cases myelomatous cells may invade the blood stream, and they may occasionally simulate myeloid leukemia; but it should be emphasized that multiple myeloma presents a characteristic clinicoanatomic picture, centered around the skeletal manifestations of the disease and their sequelae, and that with few exceptions this picture is readily distinguishable from that presented by any of the other neoplasms of hemopoietic derivation. The diagnostic significance of hypercalcemia, hyperglobulinemia and Bence-Jones proteinuria, the not infrequent presence of atypical amyloidosis in association with myeloma and the well known cytologic renal changes of almost pathognomonic distinctiveness are stressed. It is suggested that multiple myeloma is a disease of unitary cell type, the variations in cytologic appearance reflecting stages in the maturation of the basic tumor cell. Marrow obtained by sternal puncture is often an aid to diagnosis. The average length of survival after the onset of symptoms is not likely to be more than two years, but in occasional patients the course of the disease may be protracted over ten years or more. Problems in therapy are concerned mainly with palliation, particularly the relief of distressing bone pain, general supportive measures and the handling of such complications as fractures and compression of the spinal cord.

Lipophage Deposition in Atherosclerosis.—Gordon carries to its logical conclusion the theory of Leary that atherosclerosis is caused by lipophages. It is pointed out that these cells, as all cells, would normally be in the center or axial current of the blood; that with slowing of the blood stream these cells would move into the peripheral or marginal stream and come into contact with the endothelium; that, because of their lightness, they would do so before any other cell and then, because of their relative inertness, would be passively pushed into the intima by the blood pressure. Once inside the intima the majority would be retained there by the internal elastic membranes, which are impermeable to these fat cells. Atheroma is mainly a disease of the elastic arteries: as they are filled only in systole and are partially emptied during the whole cardiac cycle, the current has a certain intermittency which is less manifest in other vessels that are farther from the heart. The disease also occurs in the elastic arteries; as they dilate with age or with disease, the velocity of the blood in them is further reduced. The disease does not occur in other vessels because the current is less intermittent, the impelling power pushing the lipophage into the intima; i. e., the blood pressure is less and the internal elastic lamellas are either less well developed or do not exist. Much of the experimental work of the last few years is discussed in the light of this hypothesis.

Bulletin of Johns Hopkins Hospital, Baltimore

81:79-161 (Aug.) 1947

Symposium on Vagotomy for Peptic Ulcer: I. Experimental Observations. H. N. Harkins, D. H. Hooker, T. C. Alford Jr. and others.—p. 79.
*Id.: II. Early Surgical Results in 43 Cases. T. N. P. Johns and W. E. Grose.—p. 92.
Medical Aspects on Vagotomy for Peptic Ulcer Including Observations on Clinical Value of Insulin Test and on Postoperative Criteria for Completeness of Bilateral Gastric Vagus Section. M. Paulson and E. S. Glasden.—p. 107.
Experimental Investigation of Peptic Ulcer. E. M. Hanrahan.—p. 131.

Surgical Results of Vagotomy.—According to Johns and Grose vagotomy for peptic ulcer has been performed in 43 patients at Johns Hopkins Hospital. The 1 postoperative death which occurred was not related to vagotomy. Of the 41 patients who have been followed for from two to twenty-four months, 34 obtained satisfactory results and in 7 the results were unsatisfactory. In the satisfactory group the disappearance of ulcer pain has been striking and has overshadowed other troublesome, though transient, effects of vagotomy. These, in order of frequency, have been (1) an increase in the number of daily stools with occasional diarrhea, (2) postprandial fulness and (3) occasional postoperative vomiting, the latter two effects being related to the motor paralysis of the stomach which followed vagotomy in 24 patients. In the unsatisfactory group 2 patients have come to reoperation, 1 for recurrence of ulceration and 1 for intractable gastric retention and dilatation due to vagotomy motor paralysis. There are 2 patients in this group who have continued to show uncontrolable signs of severe gastroplegia and who may need gastroenterostomy in the future. All the failures were in patients who had vagotomy without any additional operative procedure, either plastic or ablative, on the stomach itself. The results have been uniformly satisfactory in the 24 patients who went under some such procedure in addition to vagotomy. Most satisfactory of all have been the 10 patients who had gastroenterostomy or pyloroplasty along with vagotomy.

Bull. of U. S. Army Med. Dept., Washington, D. C.

7:819-910 (Oct.) 1947

Role of Unit Surgeon: Note on Value of Brief Psychotherapy at Sick Call. B. H. Stone.—p 845.
Care of Common Cold. A. C. Randolph.—p. 857.
Physical Factors in Air Evacuation. F. L. Duff.—p. 860.
Army Neurosis Center. W. H. Dunn and H. Selinski.—p. 868.
Streptomycin in Treatment of Tuberculosis. G. W. Fishburn, M. W. Fisher and J. B. Wallace.—p. 876.
Use of Furmethide in Postoperative Urinary Retention. J. J. Toland III. —p. 879.
Need for Wider Knowledge of Preventive Medicine. F. M. Foote. —p. 887.
The Paraplegic. E. Ginzberg and H. Klarman.—p. 892.

Canadian Medical Association Journal, Montreal

57:315-418 (Oct.) 1947

Newer Antihistamines. C. H. A. Walton.—p. 323.
New Therapeutic Approaches in Allergy. R. F. Hughes.—p. 323.
*Biochemical Changes in Hypertension. Frances L. Selye.—p. 325.
Iodine Deficiency Disease. W. N. Kemp.—p. 330.
*Effect of Malaria on Pregnancy. D. D. Kulesar.—p. 332.
X Ray in Rupture of Uterus. G. W. Mylks Jr.—p. 337.
Operation for Closure of Patent Ductus Arteriosus. W. T. Mustard. —p. 340.
Uterine Inertia. H. F. P. Grafton.—p. 341.
Anesthesia for Chest Surgery. R. H. Holbrook.—p. 346.
*Intravenous Procaine. K. A. Kraft.—p. 350.
Practical Applications of Hormone Therapy in Gynecology. P. M. F. Bishop.—p. 353.
X Ray Survey of Eskimos. H. S. Lewis and G. J. Wherrett.—p. 357.
Treatment of Hyperthyroidism. G. Crile Jr.—p. 359.
Rh Factor. W. S. Stanbury.—p. 363.
Acute Intestinal Obstruction. D. S. Macnab.—p. 371.
Studies on Amebiasis. M. J. Miller.—p. 373.
Survey of Intestinal Parasites in Repatriated Prisoners of War from Hong Kong. H. Starkey.—p. 377.

Biochemical Changes in Hypertension.—Selye's studies were undertaken in an attempt to assess the part played by the adrenal cortex in hypertension. Thirty-eight patients with diastolic blood pressures ranging from 89 to 150 were studied

with regard to their electrolyte pattern. A table, in which 17 normal and 38 hypertensive sodium/chloride ratios are plotted against diastolic blood pressure, reveals that an increase in diastolic pressure is accompanied by an increase in sodium/chloride ratio, and that there are no patients in whom an increased ratio was present with a normal blood pressure. The author suggests that this increase in pressure is related to an abnormal adrenal cortical hormone production. Nearly a third of the hypertensive patients under the age of 50 give a previous history of one or more episodes of febrile arthritis, diagnosed in most cases as rheumatic fever. Some hypertensive patients manifest an increased glycocorticoid urinary excretion and this is accompanied by a decrease in urinary 17-ketosteroids. In patients exhibiting an increased sodium/chloride ratio, as well as in some not showing it, encouraging results have been obtained with ammonium chloride therapy.

Malaria in Pregnancy.—Kulcsar studied the effects of malaria on the course of pregnancy on the basis of 360 admissions to the obstetric wards of the Kweilin Provincial Hospital in China. There were 59 plasmodium-positive patients, representing 17 per cent of the total admissions; another 48 per cent had a definite past history of malaria. Nearly half of those who were plasmodium positive had complications as against 18 per cent of those who were free from malaria. Complications occurred in the form of abortions, premature labor and stillbirths. Contrary to previous reports malaria does not seem to be a serious predisposing factor to toxemias. Falciparum and vivax infections appeared to cause the same percentage of total complications, but falciparum caused more premature labors and more stillbirths. The author suggests that it might be advisable to investigate the effect of suppressive antimalarial treatment in order to prevent recurrences during pregnancy, labor and the puerperium.

Intravenous Procaine.—Kraft says that procaine has been used intravenously at his hospital since December 1944 in a total of 870 cases. It has been employed in all types of anesthesia, i. e., spinal, spinal "pentothal," nitrous oxide, ethylene, cyclopropane, cyclopropane-nitrous oxide inhalation; intravenous "pentothal" and balanced "pentothal"-cyclopropane. The procaine for intravenous use has been used in a 1:1,000 solution prepared by adding 1 Gm. of procaine to 1,000 cc. of isotonic sodium chloride solution, 5 per cent dextrose in isotonic sodium chloride solution or distilled water. The 1:1,000 solution is preferred because "pentothal," analeptics, curare or d-tubocurarine can be added to the solution or injected into the tubing without danger of an injurious precipitate being formed. The author describes the intravenous use of procaine with various anesthetic technics, giving illustrative case histories. He stresses that intravenous administration of procaine is a prophylactic and rapidly effective therapeutic measure for the prevention and correction of cardiac arrhythmias associated with cyclopropane anesthesia. Reduction of the gaseous agents and of the dosage of spinal drugs and intravenous "pentothal" can be accomplished by the intravenous use of procaine, particularly in patients who are poor surgical risks. The postoperative interval can be better balanced by intravenous procaine, in that postoperative pain is alleviated and opiate sedation is not always necessary.

Cancer Research, Baltimore

7:193-272 (April) 1947

Protein-Chemical Aspects of Cancer. G. Toennies.—p. 193.
On the Fate of Carcinogenic Hydrocarbons in Animal Body. L. T. Larionow.—p. 230.
*Induction of Ovarian Tumors in Mice by X-Rays. J. Furth and M. C. Boon.—p. 241.
Transplantable Luteoma in Mice and Associated Secondary Changes. J. Furth and H. Sobel.—p. 246.
Tumors Induced in Mice with p-Diazoaminobenzene. A. H. M. Kirby. —p. 263.

Induction of Ovarian Tumors by Roentgen Rays.—According to Furth and Boon, the production of ovarian neoplasms in female mice by roentgen rays was described in 1936. The tumors arose about seven to ten months following irradiation with single or multiple doses of 200 to 400 r. The authors cite a number of questions still awaiting solution in connection with this problem and then describe additional investigations. They found that following irradiation of mice four to six weeks of age with 87 r, 175 r or 350 r, ovarian tumors began to appear when the mice were about eleven months of age. The frequency of these neoplasms increased with time, and in almost every mouse that lived seventeen months there developed a unilateral or bilateral ovarian growth, irrespective of the dose of radiation. These ovarian growths are compared with the hyperplastic nodules that result from implantation of normal ovaries into the spleens of castrated mice. It is concluded that the latter are not autonomous neoplastic growths (although they sometimes give rise to true neoplasms), while the roentgenologically induced ovarian growths are readily transplantable autonomous growths.

Endocrinology, Springfield, Ill.

41:111-205 (Aug.) 1947

Biochemical Effects of Injections of Sex Hormones into Hypophysectomized Rats. K. W. Buchwald and Leona Hudson.—p. 111.
Studies on Indices and Causes of Prolificacy in Rats. H. H. Cole and R. B. Casady.—p. 119.
Effect of Adrenalectomy on Mammary Gland of Castrated and Estrogen Treated Castrated Male Rat. J. J. Trentin and C. W. Turner.—p. 127.
Adrenal Cholesterol and Ascorbic Acid Contents After Injury. S. Ludewig and A. Chanutin.—p. 135.
Effect of Diethylstilbestrol on Anterior Hypophysis of Thyroidectomized Rats. B. L. Baker and N. B. Everett.—p. 144.
Bio-Assay for Minute Amounts of Progesterone. C. W. Hooker and T. R. Forbes.—p. 158.
Relationship of Diet to Effect of Adrenocorticotrophic Hormone upon Urinary Nitrogen, Glucose and Electrolytes. D. J. Ingle, Mildred C. Prestrud, Choh Hao Li and H. M. Evans.—p. 170.
Gonadotrophic Hormone: Protection Against Inactivation. W. O. Maddock and C. G. Heller.—p. 177.
Effect of Gonadotrophins on Cholesterol Content of Testes of Immature Rats. J. Tepperman and Helen M. Tepperman.—p. 187.

Florida Medical Association Journal, Jacksonville

34:123-180 (Sept.) 1947

Common Fungous Diseases of Skin. W. W. Wilson.—p. 151.
Manchester Operation in Treatment of Uterine Prolapse. C. J. Collins, L. Pohlman and G. Sanchez.—p. 155.
Masculinizing Tumor of the Ovary: Report of a Case. W. J. Jennings. —p. 160.
Bromide Intoxication. W. P. Logan.—p. 161.

34:181-240 (Oct.) 1947

Curare. T. E. Daly.—p. 207.
Socialized Medicine. H. D. Van Schaick.—p. 212.
Appendectomy and Care of Appendix Stump. R. H. Center.—p. 218.

Gastroenterology, Baltimore

9:237-334 (Sept.) 1947

Peptic Ulcer: A Diagnostic and Therapeutic Problem. Sara M. Jordan. —p. 237.
*Esophageal Hiatus Hernia. F. F. Radloff and R. L. King.—p. 249.
Digestive Diseases Observed in General Hospital in Mediterranean Theater. C. J. W. Wilen and P. P. Poole.—p. 253.
Total Solids, Fat and Nitrogen in Feces: III. Study of Normal Persons Taking a Test Diet Containing Moderate Amount of Fat; Comparison with Results Obtained with Normal Persons Taking a Test Diet Containing Large Amounts of Fat. E. E. Wollaeger, M. W. Comfort and A. E. Osterberg.—p. 272.
Effect of Gastric Antacids on Gastric Secretion as Observed in the Cope Pouch Dog: Sodium Bicarbonate, Aluminum Hydroxide Gel, Calcium Carbonate, Magnesium Oxide, and Sodium Citrate. B. B. Clark and W. L. Adams.—p. 284.
Oxidative Metabolism of Mouse Stomach. H. W. Davenport.—p. 293.

Esophageal Hiatus Hernia.—Radloff and King analyzed 50 instances of herniation of the stomach through the diaphragm. Most of these hernias were discovered during a medical survey for suspected disorders of the thorax and gastrointestinal tract. Many were studied fluoroscopically on several occasions at intervals of two to three months. In more than two thirds of these patients concomitant disease was found and was often responsible for the symptoms. The predominating symptoms could be ascribed to the hiatus hernia in less than a third of the patients. Correction of the coexisting disease, reduction in weight and treatment of the underlying emotional factors afforded relief from symptoms in most cases. Surgery was necessary in only 3 cases. The author concludes that diaphragmatic hernia is usually discovered accidentally. As a rule it causes no symptoms. When it does, conservative measures usually suffice, surgery is rarely necessary.

Hawaii Medical Journal, Honolulu

7:1-92 (Sept.-Oct.) 1947

*Promin and Other Sulfones in Leprosy—Preliminary Report. N. R. Sloan.—p. 19.
Rhinoscleroma: Report of First 2 Cases Recognized in Hawaii. H. E. Crawford and M. Gerundo.—p. 23.
Acute Suppurative Appendicitis in Measles. R. L. Hill.—p. 29.
Management of Allergic Patient. T. Nelson.—p. 34.

"Promin" and Other Sulfones in Leprosy.—Sloan of the Kalaupapa settlement for leprosy patients in Hawaii says that 1943 was a turning point in the treatment of leprosy because in that year "promin," a sulfone drug (sodium p,p′-diaminodiphenylsulfone-N,N′-didextrose sulfonate), was found to effect considerable improvement in 15 of 22 leprosy patients at the leprosarium in Carville, La. Since "promin" had certain disadvantages other sulfones, particularly "diasone" (disodium formaldehyde sulfoxylate diaminodiphenylsulfone) and "promizole" (4,2′-diaminophenyl-5′-thiazolylsulfone) have been given a trial. "Promizole" seems to be less toxic; however, its production is difficult and expensive, and it may not be on the market for a long time. At the settlement in Kalaupapa "promin," "diasone" and "pyricidin" (also a sulfone drug) are being used. "Promin" has been in use for eleven months and is showing encouraging results. Improvement with "pyricidin" is less definite. "Diasone" has not as yet been in use long enough to judge its value. Highly encouraging reports on the use of "promin" and "diazone" have been made by workers in other parts of the world.

Journal of Clinical Investigation, Boston

26:827-1048 (Sept.) 1947. **Partial Index**

Plasma Non-Protein Nitrogen Distribution and Its Correlation with Efficacy of Fluid Replacement Therapy Following Thermal Injury. O. Rosenthal and M. D. McCarthy.—p. 827.
Conjugated, Non-Protein, Amino Acids of Plasma. H. N. Christensen, Eleanor L. Lynch, D. G. Decker and J. H. Powers.—p. 849.
Studies of Blood Volume in Tetralogy of Fallot and in Other Types of Congenital Heart Disease. W. Nelson, H. S. Mayerson, J. H. Clark and C. Lyons.—p. 860.
*Relation Between Serum Urea Concentration and Protein Consumption of Normal Individuals. T. Addis, E. Barrett, L. J. Poo and D. W. Yuen.—p. 869.
Serum Creatinine Concentration of Normal Individuals. Evalyn Barrett and T. Addis.—p. 875.
Correlation Between Albumin and Alpha Globulin Contents of Plasma. B. F. Chow.—p. 883.
Biochemical and Hemodynamic Changes Following Subcutaneous Injection of Glucose Solution. T. S. Danowski, A. W. Winkler and J. R. Elkinton.—p. 887.
Concentration of Protein in Samples of Normal Urine Measured by its Surface Activity. R. Gunton and A. C. Burton.—p. 892.
Renal Clearance of Penicillins F, G, K and X in Rabbits and Man. H. Eagle and E. Newman.—p. 903.
Chemical, Clinical and Immunological Studies on Products of Human Plasma Fractionation: XXXV. Persistence of Fibrin Film in Tissue and its Modification by Heat Treatment. P. R. Morrison and M. Singer.—p. 929.
*Effects of Continuous Pressure Breathing on Kidney Function. D. R. Drury, J. P. Henry and J. Goodman.—p. 945.
Liver Blood Flow in Pregnancy—Hepatic Vein Catheterization. E. W. Munnell and H. U. Taylor Jr.—p. 952.
Experimental Transmission of Minor Respiratory Illness to Human Volunteers by Filter-Passing Agents. J. H. Dingle and others.—p. 957.
Transport and Excretion of Uric Acid in Man. W. Q. Wolfson, R. Levine and M. Tinsley.—p. 991.
Importance of Volume and of Tonicity of Body Fluids in Salt Depletion Shock. J. R. Elkinton, A. W. Winkler and T. S. Danowski.—p. 1002.
Proteins in Colloidal Gold Reaction. J. Bernsohn and E. K. Borman.—p. 1026.
Effect of Local Cooling on Filtration and Absorption of Fluid in Human Forearm. Ellen Brown, C. S. Wise and E. O. Wheeler.—p. 1031.
Abnormal Renal Tubular Back-Diffusion Following Anuria. J. Redish, J. R. West, Betty W. Whitehead and H. Chasis.—p. 1043.

Serum Urea and Protein Consumption.—Addis and associates found that the average of two hundred and eighty-eight determinations of the urea concentration in the blood of 10 medical students was 53 mg. per hundred cubic centimeters. When the subjects took 0.5 Gm. of food protein per kilogram of body weight the average of a hundred and eight blood urea concentration determinations was 19 mg. On a diet containing 1.5 Gm. of protein per kilogram the average of sixty determinations was 39 mg. When 2.5 Gm. of protein per kilogram was taken, the average of one hundred and eight determinations was 45 mg. Theoretically it is now possible to predict the urea clearance of any ambulatory patient whose protein consumption is known. The theory involves the assumption that the rate and variability of endogenous protein catabolism in patients with renal disease is similar to that which existed in this normal sample. The supposition has not been tested.

Effects of Pressure Breathing on Kidney Function.—According to Drury and his associates continuous pressure breathing is a technic developed to increase the alveolar oxygen tension by breathing oxygen at higher than ambient pressure. As the extra pressure is increased, evidence of a deleterious effect on the circulation becomes apparent. At pressures of 25 to 40 mm. of mercury circulatory collapse and fainting become frequent. When using these higher pressures not only is much blood pooled in the veins of the arms and legs but also there is progressive hemoconcentration due to the passage of fluid from the blood stream into the tissue spaces. In studying the changes in blood pressure which occur during continous pressure breathing determinations on the arm proved unsatisfactory. The authors attempted to investigate changes in renal function produced by pressure breathing. Four subjects were submitted to thirty minute periods of continuous pressure breathing at 10, 20, 30 and 40 mm. of mercury above ambient pressure. They showed a progressive reduction of renal function which, with the higher pressures, fell to approximately 20 to 50 per cent of normal values. This depression in function persisted for one to two hours after the cessation of the pressure breathing. These results support the view that estimations of renal function may be used as a measure of the circulatory stress induced by a reduction of effective blood volume. It is suggested that pressure breathing should be investigated as a test of circulatory fitness by employing estimations of disturbance of renal function as an index of the extent of its effect on the circulatory system.

Journal of Experimental Medicine, New York

86:267-356 (Oct.) 1947

Studies on Conglutination Reaction, with Special Reference to Nature of Conglutinin. A. S. Wiener, Jane G. Hurst and Eve B. Sonn-Gordon.—p. 267.
Fine Structure of Clots Formed from Purified Bovine Fibrinogen and Thrombin: Study with Electron Microscope. C. V. Hawn and K. R. Porter.—p. 285.
Relative Pressures Within Cutaneous Lymphatic Capillaries and Tissues. P. D. McMaster.—p. 293.
Susceptibility of Infant Rhesus Monkeys to Poliomyelitis Virus Administered by Mouth: Study of Distribution of Virus in Tissues of Orally Infected Animals. Dorothy M. Horstmann, J. L. Melnick, R. Ward and M. J. Sa Fleitas.—p. 309.
Plasma Esterase Activity in Patients with Liver Disease and Nephrotic Syndrome. H. G. Kunkel and Sylvia M. Ward.—p. 325.
Pathogenesis of Renal Injury Produced in Dog by Hemoglobin or Methemoglobin. H. E. Harrison, H. Bunting, N. K. Ordway and W. S. Albrink.—p. 339.

Journal of Immunology, Baltimore

56:301-397 (Aug.) 1947

Effect of Tubercle Bacilli on Antigenicity of Synthetic Ester of Oleic Acid. G. Middlebrook and Rene J. Dubos.—p. 301.
In Vitro Effect of Penicillin upon Toxins of Clostridium Welchii, Type A. S. S. Schneierson.—p. 307.
*Susceptibility and Immunity in Poliomyelitis: Study of Age Incidence and Epidemicity as Related to Virgin Soil Outbreaks, Early Poliomyelitis, Geographic Distribution and Institutional Outbreaks. N. Nelson.—p. 311.
Immunization with Clostridium Septicum Toxoid and with Trivalent Gas Gangrene Toxoid. A. W. Bernheimer.—p. 317.
Antigenicity of Gas Gangrene Toxoids in Guinea Pigs, Mice and Human Beings. M. H. Adams.—p. 323.
Complement Fixation Test for Diagnosis of Human Viral Encephalitides. J. Casals.—p. 337.
Studies of Complement Fixation Reaction in Virus Systems: II. Activities of Influenza Virus Antigens and Antisera. Christine E. Rice.—p. 343.
Persistence of Antigen at Site of Inoculation of Vaccine Emulsified in Oil. Miriam Herdegen, S. P. Halbert and S. Mudd.—p. 357.
*Diagnostic Antigens for Epidemic Typhus, Murine Typhus and Rocky Mountain Spotted Fever. J. van der Scheer, E. Bohnel and H. R. Cox.—p. 365.
Quantitative Study of Passive Anaphylaxis in Guinea Pig. E. A. Kabat, G. S. Coffin and D. J. Smith.—p. 377.
Inactivation of Equine Encephalitis Virus by Mechanical Agitation. W. F. McLimans.—p. 385.

Susceptibility and Immunity in Poliomyelitis.—Nelson says that epidemics of poliomyelitis in populations previously infected show a characteristic age distribution similar to that seen in measles. In densely populated areas the age distribu-

tion is lower than in rural areas. The early history of poliomyelitis was characterized by its occurrence chiefly in young children and by the absence of epidemics. From this it may be deduced that the effective spread of the virus was exceedingly high, that infection in the vast majority of instances took place at an early age, that large concentrations of susceptible persons were not built up, and that among those infected at that early age a low percentage contracted recognizable disease. It is an interesting corollary that with improvements in general hygiene and sanitation in the past fifty years the disease has attacked an older age group and has at the same time become an epidemic disease. In a group in which sanitary conditions were extremely low the occurrence of a case of poliomyelitis was not followed by other cases, whereas in a college with the highest standards of sanitation, 24 cases occurred in a student body of 704. It seems that the earlier the age at which infection with the virus of poliomyelitis takes place, the less serious is the disease produced. Paradoxically, it may well be that the incidence of poliomyelitis has actually been increased while the general rate of infection was being cut down through better hygiene and sanitation by moving the age of infection into the older age groups.

Diagnostic Antigens for Rickettsial Diseases.—Van der Scheer and his associates point out that in complement fixation tests with antigens derived from infected tissue material the possibility of nonspecific reactions with nonrelated types of serums have to be considered. Epidemic typhus and murine typhus vaccines prepared from infected yolk sacs by the ether extraction process give nonspecific reactions in complement fixation tests with Wassermann-positive human syphilitic serums if the technic of fixation for eighteen hours at icebox temperature is used. Purified and concentrated soluble antigens were prepared from epidemic typhus, murine typhus and Rocky Mountain spotted fever vaccines by further treating the ether-extracted preparations with benzene followed by precipitation with sodium sulfate. The resulting purified soluble antigens gave little or no reaction with human syphilitic serums using complement fixation at icebox temperature. Complement fixation tests with the purified and concentrated soluble antigens clearly differentiate cases of epidemic and murine typhus from Rocky Mountain spotted fever and will often, but not always, distinguish between epidemic and murine typhus cases.

Journal of International College of Surgeons, Chicago

10:481-628 (Sept.-Oct.) 1947. **Partial Index**

Arnold Jirasek, Czech Surgeon and Neurosurgeon. L. F. Plzak.—p. 483.
Neurosurgical Team. A. Verbrugghen.—p. 487.
Clinical Significance of Proteins and Amino Acids in Surgery. W. S. Hoffman.—p. 492.
*Rupture of Cervical Intervertebral Disks. R. G. Spurling.—p. 502.
Training of the Neurosurgeon. P. Bailey.—p. 510.
*Liver Function in Surgery. K. A. Meyer, H. Popper and F. Steigmann.—p. 513.
*Control of Hemorrhage by Gelatin Sponge. H. P. Jenkins.—p. 521.
*Direct Anastomosis Between Pancreatic Cyst and Intestinal Tract. Z. Kunc.—p. 529.
Diaphragmatic Hernia. H. J. Dvorak.—p. 541.
Present Status of Pancreaticoduodenectomy for Carcinoma of Ampulla of Vater and of Head of Pancreas. J. T. Reynolds and W. Marlowe.—p. 544.
Pelvic Sympathectomy. H. C. Voris and H. E. Landes.—p. 553.
Congenital Lung Cysts: Pathologic Characteristics and Importance of Recognition. W. E. Adams.—p. 558.
Anastomosis of Aorta to Pulmonary Artery for Relief of Congenital Pulmonary Stenosis. W. J. Potts.—p. 569.
Use of Propylthiouracil in Hyperthyroidism. A. S. Jackson.—p. 576.
Some Clinical Entities Frequently Misdiagnosed. H. Bailey—p. 579.
Intrapericardial Sarcoma. R. Nissen.—p. 588.
Treatment of Fractures of Ankle Joint. C. L. Hall and C. Berg.—p. 592.
Partial Colectomy with Partial Hepatectomy: Carcinoma of Splenic Flexure with Solitary Liver Metastasis. P. Thorek.—p. 606.

Ruptured Disks.—Spurling reports 32 cases of lateral rupture of the lower cervical intervertebral disks with radicular pain affecting the upper extremity. The clinical syndrome is remarkably constant and easily recognized. Accurate localization of the lesion on clinical observations is usually possible. The diagnostic features of lateral rupture of the fifth cervical disk are as follows: there is pain radiating from the neck into the shoulder and arm with paresthesias into the posterior aspect of the thumb. Symptoms are always aggravated by tilting the head to the painful side. Weakness or absence of the tendon reflex of the biceps brachial muscle is demonstrable on neurologic examination. Lateral rupture of the sixth cervical disk produces pain radiating from the neck into the shoulder and arm with paresthesias into the index, middle and perhaps the ring finger and tip of the thumb. These symptoms may be aggravated likewise by tilting the head to the painful side. The lesion is associated with weakness or absence of the tendon reflex of the triceps brachial muscle. "Pantopaque" myelography is an exceedingly accurate method of diagnosing ruptured cervical disks. Conservative treatment may relieve symptoms in many cases. When conservative measures fail, operative removal of bone is justified on the basis that it is a simple, safe procedure and the results are excellent.

Liver Function in Surgery.—Meyer and his co-workers analyze a series of liver function tests performed in 95 cases of surgical jaundice. In 42 cases the extrahepatic biliary obstruction resulted from a malignant process and in 53 cases from a benign process. The tests are divided into those indicating impairment of liver cell function and those indicating interference with the flow of bile. In most cases hepatic damage was principally due to prolonged biliary obstruction itself (biliary hepatitis) and less often due to associated bacterial infection of the portal triads (purulent hepatitis). As a rule, more tests for liver cell damage and more tests for impaired bile flow are positive in malignant obstruction than in benign obstruction. The presence of liver cell damage, as indicated by function tests (at least two of these tests were positive in 59 of the authors' cases of surgical jaundice) does not contradict the diagnosis of surgical jaundice. If other criteria indicate the presence of an extrahepatic biliary obstruction, the demonstration of liver function impairment increases the urgency for surgical intervention.

Hemostasis by Gelatin Sponge.—Jenkins used the gelatin sponge in experimental studies on dogs ("gelfoam") to control hemorrhage from wounds of the liver by holding a "blanket" of this material over the bleeding surface of the organ. A wound was made in the vena cava, and the resulting profuse hemorrhage was controlled by the application of a "patch" of gelatin sponge held on the bleeding vessel. The same technic was used to control hemorrhage from experimental wounds of the heart. A through and through wound was made in the aorta with a scalpel, and the hemorrhage was controlled by a "cuff" of dry compressed gelatin sponge, which was wrapped about the vessel and supported by a sheath of chromic catgut. The effectiveness of this hemostatic agent alone under these rather critical experimental conditions demonstrated its potential value in clinical surgery. The sponge acts to a considerable extent as a tampon which slows or stops the flow of blood, thus permitting the clotting mechanism of the blood to become more effective. The clotting of the blood in the sponge and the adherence of the sponge to the wound due to the liberation of fibrin produces essentially a reenforced clot. The gelatin sponge undergoes absorption with nominal tissue reaction after the hemorrhage is controlled and the wound is healed. The careful and judicious use of gelatin sponge should provide the surgeon with a useful technical method for controlling hemorrhage where ligatures or sutures may not be adequate, feasible or desirable. Clinical observations which have thus far been made support this view.

Surgical Treatment of Pancreatic Cyst.—Kunc treated 3 patients, 2 men aged 51 and 40, respectively, and 1 woman aged 45 with pancreatic pseudocysts by direct anastomosis of the cyst to the stomach or duodenum. In 1 patient there were two pseudocysts, one in the head and the other in the tail of the pancreas, which were not interconnected. The largest cyst had a content of 8 liters, the smallest, 75 cc. In 2 patients a transstomachic operation after Jurasz was performed. In the third patient one cyst was connected to the stomach by the Jurasz technic and the other transduodenally to the duodenum by the Kerschner technic. The results were satisfactory in all cases. The concept of the Jurasz and the Kerschner operation is the prevention of pancreatic fistula formation. Roentgenographic examination carried out early after the operation suggests that after primary anastomosis reflux of the gastrointestinal contents into the pancreatic cysts and ducts is inhibited by a spasm

at the site of the anastomosis. Through peristalsis of the alimentary tract, a sucking effect is exerted on the contents of the cyst, which consequently contracts rapidly. There was not much bleeding, although all the pseudocysts were fresh and associated with considerable necrosis. On comparing the postoperative course and the final results in these 3 patients with those in patients operated on by other methods, primary anastomosis to the stomach or duodenum may be considered as the method of choice in the surgical treatment of all pancreatic cysts and pseudocysts.

Journal of Lab. and Clinical Medicine, St. Louis

32:1045-1168 (Sept.) 1947. **Partial Index**

Morphologic Changes in Lymphocytes of Persons Exposed to Ionizing Radiation. Annamae Dickie and L. H. Hempelmann.—p. 1045.
Studies on Lymphogranuloma Venereum: Evaluation of Complement Fixation Test with Lygranum. M. F. Shaffer and G. Rake.—p. 1060.
Coagulation Time of Blood Heparinized in Vitro: Correlation of Results with Those of Heparin Tolerance Test. A. B. Hagedorn and N. W. Barker.—p. 1087.
New Method for Indirect Measurement of Blood Pressure in the Rat. H. Kersten, W. G. Brosene Jr., F. Ablondi and Y. SubbaRow. —p. 1090.
Diagnosis of Pancreatic Disease by Enzyme Tests. L. M. Morrison. —p. 1107.
Intravenously Administered Gelatin—Toxicity Study. M. J. Vander Brook, S. C. Lyster, B. E. Graham, N. E. Pomeroy and G. F. Cartland.—p. 115.
*Attempts at Experimental Production of Arthritis. R. Pemberton, J. Eiman, F. M. S. Patterson and Eleanor A. Stackhouse.—p. 1121.

Experimental Arthritis.—Pemberton and his associates say that relation of the endocrine system to the phenomena of arthritis has long been suspected. Efforts have been made to simulate in experimental animals the phenomenon of arthritis in some of its manifestations by means of injection of hormonal material, by the ablation of certain hormone-yielding organs and by other steps. The authors give particular attention to observations of Selye. Summarizing their own results with similar experiments they have noted arthritic-like lesions in groups of rats maintained on standard laboratory rations and on grossly unbalanced diets and in animals receiving injections of massive doses of desoxycorticosterone acetate. In one group receiving massive doses of desoxycorticosterone acetate, together with a 1 per cent solution of sodium chloride for drinking water, articular changes were formed in 50 per cent of young female white rats. These results are at variance with the observations of certain other workers that arthritic lesions are seldom seen in intact desoxycorticosterone-treated rats. Attempts to increase the incidence and severity of these arthritic-like lesions by exposure to cold, by thyroidectomy, adrenalectomy and gonadectomy were unsuccessful. The changes observed in the joints are those of focal areas of degeneration and ulceration in the articular cartilages.

Journal of the Mount Sinai Hospital, New York

14:133-848 (Sept.-Oct.) 1947. **Partial Index**

Contribution to Study of Tubal Patency by Kymographic Insufflation. L. Bonnet.—p. 141.
Utero-Tubal Insufflation in Uterine Malformations. O. Jurgens.—p. 199.
Ectopic Pregnancy: Study of 174 Cases. W. C. Danforth.—p. 269.
Repair of Intractable Rectovaginal Fistula: New Procedure. J. H. Garlock.—p. 302.
Hypophysio-Hypothalamic Interfunctions and Dysfunctions. J. H. Globus, A. I. Goldfarb and S. Silver.—p. 308.
The Huhner Test. M. Huhner.—p. 388.
Recent Biologic Investigations and Their Significance for Pathology. P. Klamperer.—p. 442.
Development of Surgical Treatment of Gastric and Duodenal Ulcer During Last Forty Years. R. Lewisohn.—p. 470.
Epithelioma of Uterine Cervix. J. C. Masson and D. B. Judd.—p. 483.
Venous Thrombosis and Pulmonary Embolization in Obstetrics and Gynecology. H. Neuhof.—p. 520.
Presacral Neurectomy in Intractable Dysmenorrhea. L. E. Phaneuf. —p. 553.
Uterography as an Aid in Diagnosis of Uterine Bleeding. S. A. Robins. —p. 559.
Treatment of Carcinoma of Cervix Complicated by Pregnancy. G. G. Ward.—p. 674.
Reaction of Fallopian Tubes to Increased Intra-Uterine Pressure of Carbon Dioxide Gas as Determined by Kymograph. T. R. Wilson.—p. 695.
Rubin Test: Utero-Tubal Insufflation, Its Origin and Scope. S. Wimpfheimer.—p. 712.
Chorionepithelioma: Hormonal Studies and Pathologic Findings. E. Klempner.—p. 793.

Journal Pharmacology & Exper. Therap., Baltimore

91:1-92 (Sept.) 1947

Cardiovascular and Respiratory Effects of Antihistamine Agent, Beta-Dimethylaminoethyl Benzhydryl Ether Hydrochloride (Benadryl Hydrochloride). C. V. Winder and R. W. Thomas.—p. 1.
Action of Digitalis Glycosides on Central Nervous System with Special Refererce to Convulsant Action of Red Squill. H. Gold, W. Modell, McK. Cattell and others.—p. 15.
Toxic Action of Preparations Containing the Oxygen-Labile Hemolysin of Streptococcus Pyogenes: IV. Comparison of Cardiotoxic Action with That of Saponin. G. L. Cantoni and A. W. Bernheimer.—p. 31.
Metabolic Action of Cardiac Glycosides: I. Influence of Respiration of Heart Muscle and Brain Cortex. A. Wollenberger.—p. 39.
*Tests for Chronic Toxicity of Propylene Glycol and Triethylene Glycol on Monkeys and Rats by Vapor Inhalation and Oral Administration. O. H. Robertson, C. G. Loosli, T. T. Puck and others.—p. 52.
Effect of Di-Isopropyl Fluorophosphate on Neuromuscular Transmission. C. C. Hunt.—p. 77.
Hypoprothrombinemia Resulting from Administration of Sulfaquinoxaline. C. W. Mushett and A. O. Seeler.—p. 84.

Tests for Toxicity of Propylene Glycol and Triethylene Glycol.—Robertson and his associates exposed monkeys and rats continuously to high concentrations of propylene glycol and triethylene glycol for periods of twelve to eighteen months. Comparative observations on the growth rates, blood counts, urine examinations, kidney function tests, fertility and general condition of the test and control groups exhibited no essential differences between them with the exception that the rats in the glycol atmospheres exhibited consistently higher gains in weight. Some drying of the skin of the monkeys' faces occurred after several months' continuous exposure to a heavy fog of triethylene glycol. However, when the vapor concentration was maintained just below saturation by means of the glycostat this effect did not occur. Examination at necropsy likewise failed to reveal differences between the animals kept in glycolized air and those living in the ordinary room atmosphere. Extensive histologic study of the lungs was made to ascertain whether the glycol produced any generalized or local irritation. None was found. The kidneys, liver, spleen and bone marrow also were normal. The results of these experiments, in conjunction with the absence of ill effects in patients exposed to both triethylene glycol and propylene glycol vapors for months at a time, provide assurance that air containing these vapors in amounts up to the saturation point is completely harmless.

Kansas Medical Society Journal, Topeka

48:441-492 (Oct.) 1947

Cancer Diagnosis by Smears. W. A. Grosjean.—p. 441.
Resection of Cecum and Right Portion of Colon for Malignant Tumor. E. S. Judd Jr.—p. 444.
*Follow-Up Procedure on Cases and Suspected Cases Found in Mass X-Ray Survey. H. Mark.—p. 451.
*Pentothal and Curare for Modification of Electric Convulsions. J. D. Rising.—p. 456.

Follow-Up After Roentgen Ray Survey.—Mark shows that the survey filming is only a means of screening the apparently healthy population into two groups, (1) those with essentially normal lungs and (2) those with some abnormality. The differentiation of those with abnormal conditions requires further examinations and clinical evaluation. These patients are referred back to their physician. The prompt diagnosis of early tuberculosis, early cancer of the lung or early heart disease demands an adequate clinical follow-up, which should aim at an etiologic diagnosis and at the determination whether the disease is communicable and progressive. The author outlines the steps that must be taken to ascertain or rule out the presence of tuberculosis. In reviewing the results of 40,000 consecutive chest x-rays, he stresses the existence of many pulmonary conditions which simulate tuberculosis. There were 623 persons with abnormal roentgenologic pulmonary observations. An adequate clinical follow-up is essential to avoid the numerous diagnostic errors of the past, in which many persons were hospitalized in sanatoriums when there was not even a tuberculous infection, while others who were admitted to general hospitals or were cared for at home had frank open cases of undiagnosed pulmonary tuberculosis. The responsibility for follow-up is not entirely that of the private physician but also must be borne by the public health authorities.

"Pentothal" and Curare in Electric Convulsions.—Rising presents results of experiments which were designed to test the effectiveness and safety of "pentothal sodium," curare ("intocostrin") and mixtures of the two drugs for the modification of induced electric convulsions. Studies made on 10 dogs revealed that "pentothal" is less efficient in modifying electric convulsions than those induced with pentamethylenetrazol ("metrazol"), 10 mg. per kilogram of body weight being required in the former as contrasted with 3 mg. per kilogram for the latter. This dosage cannot be transferred directly to human medication, as the dosage of a barbiturate required to produce a specific effect in man is only one-fourth to one-half that required in dogs. "Pentothal" decreases both apnea and excitement incident to induced electric shock. Curare does not raise the convulsive threshold and is efficient in softening the seizures, but the range of therapeutic dosage is dangerously narrow. A combination of "pentothal" and curare satisfactorily modifies electrically induced convulsions, permits the use of smaller amounts of curare and is accompanied by less impairment of breathing than that which frequently follows electric shocks preceded by therapeutic doses of curare.

Kentucky Medical Journal, Bowling Green

45:357-391 (Oct.) 1947

Cancer Control. G. Aud.—p. 364.
Surgical Horizons. J. D. Hancock.—p. 369.
The American Medical Association. G. F. Lull.—p. 372.
Common Causes of Blindness. J. W. Harned Jr.—p. 379.

Missouri State Medical Assn. Journal, St. Louis

44:713-784 (Oct.) 1947

Uterine Ring Dystocia. H. W. Johnson.—p. 729.
Diagnosis and Treatment of Lesions of Bronchial Tree. A. M. Olsen. —p. 731.
Some Clinical Experiences in European Theater of Operations. W. S. Middleton.—p. 735.
Nutritional Defficiencies as Cause of Disease. W. H. Griffith.—p. 738.
*Some Nutritional Pitfalls in General Hospitals. G. G. Duncan, W. S. M. Ling, Ruth J. Floeck and Edith S. Grand.—p. 743.
Condyloma Acuminatum. M. M. Marks.—p. 749.
Studies on Translumbar Aortography: Simple Apparatus for Translumbar Aorteriography. A. E. Vitt and W. F. Melick.—p. 749.
Visualization of Maternal Circulation at Site of Placenta (Placentagrams): Preliminary Report. L. J. Hartnett.—p. 754.
*Early Postpartum Ambulation. W. L. Smiley.—p. 756.

Nutritional Pitfalls in General Hospitals.—Duncan and his associates, after calling attention to some of the nutritional hazards of hospitalized patients, stress the importance of (1) training medical students in the practical application of known principles of nutrition, which training is woefully inadequate in some medical schools; (2) the greater appreciation of and training of dietitians in the clinical aspects and problems of nutrition; (3) the coordination of the supervision by nurses, interns and dietitians in such a manner that a suitable inquiry and corrective measures may be put in operation if a patient returns an appreciable amount of food; (4) the constant alertness of visiting physicians to the nutritional status of their patients combined with free discussion with hospital personnel of these problems in the presence of the patient, and (5) the alertness to changes in the understanding of nutrition, being ever ready to reevaluate existing data in the face of new discoveries.

Early Postpartum Ambulation.—Smiley's observations on 514 puerperal women revealed that the following were the outstanding advantages obtained from early ambulation: 1. There was improvement in the feeling of well-being and delight in being able to walk about and to go to the bathroom, thus eliminating the use of the bed pan. 2. The staff was impressed by the lack of bladder and bowel disturbances. Reduction in the number of catheterizations and enemas to be given was a boon to the nursing staff, which was left free for special duties on the more serious cases. 3. Failure to find an increase in subinvolution, or retrodisplacement, and the satisfactory healing of perineal wounds was evidence of the safety of the regimen. There is an increase in the lochial flow during the earlier days; the patients should be told before-hand that this will occur but will cease in from eight to ten days and that they need have no fear because of the increased bleeding on first arising. Relaxations usually do not develop until ten to fifteen years after the first pregnancy. Therefore it is impossible to say as yet whether they will increase after early ambulation, but there seems to be little reason to expect this.

New England Journal of Medicine, Boston

237:501-530 (Oct. 2) 1947

Comparison Between Clinical Effects of Pyribenzamine and Those of Benadryl. Mary H. Loveless and Halla Brown.—p. 501.
Acute Hemolytic Anemia in Primary Atypical Pneumonia Produced by Exposure and Chilling. R. A. Colmers and J. G. Snavely.—p. 505.
*Prefrontal Lobotomy in Chronic Depressive States of Old Age. A. Myerson and P. G. Myerson.—p. 511.
Malignant Testicular Neoplasms in Infancy: Report of Case with Six-Year Survival. A. Meltzer and B. Bloom.—p. 513.
Serum Lipids and Their Value in Diagnosis. S. J. Thannhauser.—p. 515.
Ewing Tumor of Rib and Phalanx of Toe.—p. 524.
Hematometrium Due to Cervical Stenosis.—p. 525.

Prefrontal Lobotomy in Depressive States in Old Age.—The Myersons say that mental illness in old age is usually regarded as a hopeless problem. Such patients react poorly to electric shock therapy. The authors report on 4 women, over sixty years of age, with chronic depression, whose symptoms were relieved by prefrontal lobotomy. Tension and distress were greatly alleviated, and there was no obvious intellectual impairment. The authors emphasize that old persons with chronic depression should not be regarded as hopeless and doomed to live out their remaining years in retreat and unhappiness. Properly performed, prefrontal lobotomy can do them no harm. The alternative to the operation is to add the misery of melancholia to the disabilities of old age.

New Jersey Medical Society Journal, Trenton

44:347-390 (Sept.) 1947

Control of Whooping Cough. R. P. Kandle.—p. 350.
Congenital Defect of Sternum with Congenital Heart Disease. C. Hyman. —p. 355.
General Surgery in Psychotic Patients. J. F. Kustrup.—p. 357.
Vascular Nevi and Their Treatment. A. J. Delario.—p. 360.
Prostatic-Hemorrhoidal Impotence Syndrome. H. B. Schwartz.—p. 371.
Marked Toxic Side Effect of Pyribenzamine. E. C. Kern.—p. 374.

44:391-438 (Oct.) 1947

Pulmonary Embolism and Venous Thrombosis: Diagnosis, Prophylaxis and Treatment. R. R. Linton.—p. 394.
Simulated Mental Retardation Produced by Emotional Neglect. R. N. Shapiro.—p. 401.
Erythema Multiforme as Sequela of Dermatitis Venenata. C. C. Carpenter.—p. 404.
Examination of the Sterile Couple. D. B. Roth.—p. 407.
Homologous Serum Jaundice Following Use of Surplus Dried Plasma. C. F. McGinnes.—p. 410.

New York State Journal of Medicine, New York

47:2047-2142 (Oct. 1) 1947

Evaluation of Anesthesia with Pentothal Sodium, Nitrous Oxide, and Ether. P. W. Searles.—p. 2091.
Treatment of Intractable Pain. D. Stubbs and J. P. Murphy.—p. 2094.
Differential Segmental Subarachnoid Block: Diagnostic Test for Hypertension. B. Etsten and W. Schwab.—p. 2098.
Phlebitis and Pulmonary Embolism Following Pentothal-Sodium Anesthesia. H. H. Ryan Jr. and C. B. Hickcox.—p. 2102.

47:2143-2238 (Oct. 15) 1947

Intravenous Procaine: Preliminary Report. D. J. Graubard, R. W. Robertazzi and M. C. Peterson.—p. 2187.
*Prolonged Therapeutic Action of Intracaine in Painful Musculoskeletal Disorders. E. H. Bettmann.—p. 2193.
Medical Consideration of the Air Traveler. F. H. Shillito.—p. 2201.

Intracaine in Musculoskeletal Disorders.—Since 1930, Bettmann has studied various substances for their antispasmodic and analgesic effect, and in particular their toxicity and prolonged action. During the last five years he used "intracaine" (betadiethylaminoethyl *p*-ethoxy-benzoate hydrochloride) a new anesthetic agent, which was found to possess prolonged and superior anesthetic potency with almost complete absence of local toxicity. "Intracaine" in oil (5 per cent) was used in 180 patients with orthopedic and traumatic disorders. It was found especially valuable in the treatment of low back pain due to sacrolumbar and sacroiliac derangements, in fractures,

bursitis, contusions, muscle tears, myofascitis, epicondylitis, periostitis, certain ligamentous injuries, tendovaginitis and also in contractures of spastic or mechanical origin. It also benefited patients with degenerative arthritis and neuritis. Of all those treated with "intracaine" in oil, about 50 per cent were permanently free of pain and about 40 per cent were able to receive other therapy (physical manipulation, traction casts, braces) while the acute and predominant pain was controlled by the anesthetic agent. Ten per cent were not improved. "Intracaine ointment" was successfully applied for massage of painful muscles after injury and immobilization in casts. It was used with equally beneficial results in painful skin wounds and in burns, producing a prolonged and comfortable analgesic effect.

Occupational Medicine, Chicago

4:1-136 (July) 1947

Tributes to Dr. Leroy Upson Gardner. A. J. Lanza and others.—p. 1.
Employability of Silicotic Subjects: Summary of Report of Minnesota Survey. L. U. Gardner.—p. 17.
Industrial Job Placement of Persons with Inactive Tuberculosis: Guide for Employment Managers and Personnel Directors. S. Hamlin and others.—p. 22.
Solubility Theory of Silicosis: Critical Study. E. J. King.—p. 26.
Silicosis in the Gold Mines of Witwatersrand: Brief Review. A. J. Orenstein.—p. 50.
Contributions by Dr. Gardner to Pathology of Bauxite Workers' Lung. A. R. Riddell.—p. 56.
Medical Examination and Compensation of Miners for Industrial Injury: Development of System at Broken Hill, New South Wales. W. E. George.—p. 68.
Pneumonoconiosis in Coal Workers in Wales. J. Gough.—p. 86.
Report of One Year's Mycologic Investigation. A. A. Lopez.—p. 98.
First Stages of Dust Cell Formation in Pulmonary Tissue. A. Policard. —p. 100.
Significant Aspects of Exposure to Beryllium Compounds in Industry. C. R. Williams.—p. 104.
Nodulation with Superimposed Infection in Lungs of Foundry Grinders and Burners: Report of 4 Unusual Cases. L. E. Hamlin.—p. 111.

Oklahoma State Medical Assn. Jour., Oklahoma City

40:364-402 (Sept.) 1947

Modern Therapy of Sinus Disease. F. L. Lederer.—p. 366.
Treatment of Sub-Acute Bacterial Endocarditis. P. M. Schreck.—p. 369.
Parent in Pediatric Practice. H. J. Binder.—p. 372.
Mental Fatigue States, Symptoms and Diagnosis. C. R. Rayburn. —p. 375.

40:403-440 (Oct.) 1947

Current Problems in Public Health. J. F. Hackler.—p. 406.
Use of Curare in Anesthesia. H. Doudna.—p. 409.
Early Diagnosis and Treatment of Primary Pulmonary Tuberculosis in Children. J. G. Hughes.—p. 411.
Congenital Heart Disease. H. A. Ruprecht.—p. 417.

Proc. of Staff Meet. of Mayo Clinic, Rochester, Minn.

22:433-464 (Oct. 1) 1947. **Partial Index**

Cardiac Manifestations of Anxiety. H. B. Burchell.—p. 433.
Effects of War Conditions on Child Health. R. W. B. Ellis.—p. 441.
*Diagnostic Errors in Carcinoma of Large Intestine. R. J. Jackman. —p. 447.
Raynaud's Disease: Report of Case with Late Postoperative Results. A. W. Adson.—p. 450.
Preliminary Report on Experimental and Clinical Studies with Polythene Film. M. H. Brown, J. H. Grindlay and W. McK. Craig.—p. 453.
Tissue Anoxia Resulting from Respiratory Alkalosis. H. M. Carryer. —p. 456.

Diagnostic Errors in Carcinoma of Large Intestine.—According to Jackman, many patients with carcinomas of the large intestine receive treatment for some supposed condition of the rectum or colon other than the carcinoma, which thus remains undiscovered. He reviews the records of 817 patients with carcinoma of the colon and rectum who came to the Mayo Clinic during the year 1944. More than half the patients with carcinoma of the large intestine had lesions which could be palpated by digital examination of the rectum. About a fourth of the patients in this group had received some form of treatment for disease of the colon or rectum but not for the carcinoma, which was within reach of the examining finger. An additional 16.2 per cent of all patients who had carcinomas in the large intestine had lesions which were within reach of the sigmoidoscope. A fourth of this group had received treatment for some condition other than the carcinoma, which had remained undiscovered. Patients who had carcinomas beyond the reach of the examining finger and the sigmoidoscope constituted the remaining 29.5 per cent of the total series. Of these patients 232 had carcinomas which were diagnosed by roentgenograms of the colon. Twenty-three of these patients had received other treatment during the period in which they were experiencing symptoms from the carcinoma. They had been treated for hemorrhoids, pernicious anemia, colitis, appendicitis or polyps.

Psychoanalytic Quarterly, Albany, N. Y.

16:303-457 (July) 1947

Psychopathology of Social Prejudice. G. Zilboorg.—p. 303.
Problems of Therapeutic Management in a Psychoanalytic Hospital. Frieda Fromm-Reichmann.—p. 325.
Projection, Extrajection and Objectivation. E. Weiss.—p. 357.
Psychopathology of Orgasm. S. Keiser.—p. 378.
Psychological Theory of Formal Beauty. J. Weiss.—p. 391.

Quarterly J. Studies on Alcohol, New Haven, Conn.

8:197-376 (Sept.) 1947

Rorschach Study on Psychologic Characteristics of Alcoholics. Charlotte Buhler and D. W. Lefever.—p. 197.
*Psychologic Factors in Conditioned Reflex Treatment of Alcoholism. F. Lemere.—p. 261.
Social Pattern of Alcoholic Drinking. J. W. Riley Jr. and C. F. Marden.—p. 265.
Study of First Admissions with Alcoholic Psychoses in New York State, 1943-1944. B. Malzberg.—p. 274.
Medical, Legal and Social Approaches to Problems of Inebriety. Proceedings of Conference Sponsored Jointly by the Research Council on Problems of Alcohol and the New York Academy of Medicine.—p. 296.

Conditioned-Reflex Treatment of Alcoholism.—According to Lemere, aside from the obvious suggestive effect of the conditioned-reflex treatment of alcoholism, there are additional psychologic factors which are important adjuncts to effective therapy. A genuine desire on the part of the patient to stop drinking is essential for any treatment of alcoholism. The alcoholic must have reached the point in his drinking career at which the pain of drinking becomes more powerful than the pleasure of alcoholic escape before he can be treated successfully. The fact that the patient pays several hundred dollars for treatment acts as a deterrent against relapse. A hospital devoted solely to the treatment of alcoholism is highly desirable. Psychotherapy is usually limited to an attempt to help the patient solve his immediate and more obvious personal problems. Emphasis is placed on reassurance, education and the persuasive power of the physician-patient relationship. The theory that drinking is simply another symptom of neurosis is open to question in many cases. Many patients are quite stable when not drinking. An attempt is made to educate the patient to accept the fact that he must remain completely abstinent and that moderate drinking will always be impossible for him. The more extensive the follow-up the better the results of treatment.

Rhode Island Medical Journal, Providence

30:638-710 (Sept.) 1947

Certain Aspects of Problem Drinking. C. H. Durfee.—p. 651.
Is Asthma a Symptom or a Disease? F. M. Rackemann.—p. 657.
Social Work in the Aged. M. W. Thewlis.—p. 660.
Impetigo Bockhart. F. Ronchese.—p. 662.
Organizational Devices to Protect Patient. A. M. Burgess.—p. 695.

30:709-779 (Oct.) 1947

Abdominal Hysterectomies Performed at Rhode Island Hospital, 1941 Through 1945. R. E. Martin.—p. 723.
Coronary Thrombosis and Diet. F. J. Burns.—p. 727.
*Use of Choline Chloride in Cirrhosis of Liver, with Recovery After 106 Paracenteses. L. E. Burns.—p. 729.
Clinicopathological Conference: Rhode Island Hospital. C. S. Keefer and B. E. Clarke.—p. 731.
Report of Surgical Insurance Plan Study Committee of Rhode Island Medical Society to House of Delegates. R. Abbate and others.—p. 737.

Choline Chloride in Cirrhosis of Liver.—Burns records the history of a woman, aged 45, in whom cirrhosis of the liver developed as the result of extreme alcoholism and deficiencies in dietary intake. One hundred and six paracenteses were performed over a period of about two years. An average of about 6 quarts (5.7 liters) of fluid was obtained at each paracentesis. In order to replace the protein lost with paracentesis, it was

necessary to supply a tremendous daily intake of protein. The patient ate ¼ pound (113.4 Gm.) of cottage cheese at least five times weekly. She drank at least 1 quart (0.95 liter) of skim milk and ate at least ½ pound (227 Gm.) of meat a day. Liver injections, vitamin B complex and brewers' yeast tablets were given daily. Several months later a regimen of 5 grains (0.32 Gm.) of choline chloride three times a day was started. Treatment with injections of liver and vitamin B complex was continued for three years, and the choline chloride has been continued to date. Under the influence of this treatment the hepatic cirrhosis was gradually arrested and paracenteses were no longer necessary. The authors think that the earlier a high protein, high vitamin B diet plus added choline is instituted, the sooner the sick liver will be brought under control.

Southern Surgeon, Atlanta, Ga.

13:715-776 (Oct.) 1947

Free Composite Grafts of Nipples in Mammaryplasty. W. M. Adams. —p. 715.
Rational Treatment of Brain Abscess. W. G. Haynes.—p. 734.
Combined Colostomy and Miller-Abbott Tube in Preparation of Left Sided Colon Lesions for Surgery. S. W. Windham, J. T. Ellis and S. G. Latiolais.—p. 745.
Etiology, Prevention and Treatment of Vesicovaginal Fistula. V. S. Counseller.—p. 752.
*Mistaken Surgical Diagnoses in Hookworm Disease. D. McEwan, J. G. Economon and R. E. Zellner.—p. 760.
Obligations and Opportunities of Industrial Surgery. E. M. Howard. —p. 767.

Mistaken Surgical Diagnoses in Hookworm Infection.—The report by McEwan and his co-workers is based on an analysis of all cases of hookworm infection, intestinal ancyclostomiasis, in which patients were admitted to the Orange Memorial Hospital because of abdominal complaints from 1939 to 1946. Stool analysis was not a regular routine but was made only when indicated. Of 46 patients whose symptoms were sufficiently severe to warrant hospitalization, 23 have complained of abdominal pains; 12 of the 23 were admitted to the surgical service and 4 of the 12 were operated on for acute appendicitis; 1 of the 4 had a perforated appendix with generalized peritonitis. In this instance the hookworm infestation was considered to be incidental to the primary disease. The most frequent diagnosis was that of acute appendicitis, made in 9 cases; next, hookworm infection, in 6 cases; and peptic ulcer and acute salpingitis, in 3 cases each. Other diagnoses considered were as follows: nonspecific colitis, 2; acute pancreatitis, 1; acute cholecystitis, 1; bronchopneumonia, 1; pulmonary emphysema, 1; typhus, 1, and gastrointestinal allergy, 1. The surgeon should be aware of the possibility of hookworm infestation producing abdominal symptoms simulating appendicitis, peptic ulcer and other surgical diseases of the abdomen.

Surgery, St. Louis

•22:571-728 (Oct.) 1947

Sympathectomy as an Adjuvant in Operative Treatment of Aneurysms and Arteriovenous Fistulas: I. Sympathectomy Performed Before or at Time of Operation. H. B. Shumacker Jr.—p. 571.
Id.: II. Sympathectomy Performed After Operation. H. B. Shumacker Jr.—p. 597.
Repair of Skull Defects. W. G. Peacher, B. Cannon and J. B. Brown. —p. 611.
Repair of Scalp Defects. B. Cannon, J. B. Brown and W. G. Peacher. —p. 619.
Carcinoma Involving Common Bile Duct: Report of 4 Cases of Successful Resection. H. E. Leiter.—p. 627.
*Perforation of Small Intestine by Miller-Abbott Tube. L. Berger and S. Achs.—p. 648.
Surgical Management of Gastrojejunocolic Fistulas. R. F. Barber and J. L. Madden.—p. 657.
Surgical Drains Made of Vinyl Plastic Film. H. G. Bregenser and P. Gross.—p. 671.

Perforation of Intestine by Miller-Abbott Tube.—Berger and Achs discuss the advantages and disadvantages of the Miller-Abbott tube and show that although its advantages are unquestioned, intestinal intubation if used unwisely may lead to serious and even fatal complications. The authors report the case of a woman, aged 40, which illustrates a type of complication not previously reported, namely, perforation of the small intestine. The woman recovered. The case is a dramatic example of the complications which may occur from the overprolonged use of the Miller-Abbott tube in the treatment of intestinal obstruction.

Western J. Surg., Obst. & Gynecology, Portland, Ore.

55:473-524 (Sept.) 1947

Resection of Rectum and Rectosigmoid with Primary Extraperitoneal End-to-End Open Anastomosis. C. Mathewson Jr. and V. Richards. —p. 473.
Venous Thrombosis. J. M. Schmoele.—p. 481.
Manual Removal of Placenta: Report of 410 Cases of Manual Removal of Placenta with 1 Death; 150 Cases Were Done as a Routine or Prophylactic Measure. H. W. Mayes.—p. 483.
Disease of Solitary Kidney. A. H. Peacock.—p. 491.
Actinomycosis of Internal Female Genitalia: Report of 2 Cases. E. M. Baker.—p. 501.
*Testicular Biopsy in Sterile Male. F. A. Simmons and R. Sniffen. —p. 508.

Testicular Biopsy in the Sterile Male.—Simmons and Sniffen say that since 1940 200 biopsies of the human testicle have been secured and studied at the Massachusetts General Hospital. From this group 85 patients have been selected whose chief complaint was sterility. Testicular biopsy was carried out in 75 of the cases only after the wife had been found normal. Testicular biopsy is valuable in deciding whether repeated azoospermia is due to block or germ plasm failure, or in helping to differentiate between those patients who may be expected to respond to treatment and those who will not, thus saving the patient time and expense. There is little correlation between the microscopic findings and the physical examination and between the urinary hormone assays and semen study, except that all patients with too much follicle-stimulating hormone had malfunctioning tubular epithelium.

West Virginia Medical Journal, Charleston

43:323-358 (Oct.) 1947

*Endemic Typhus Fever: Clinical Study of 24 Cases: Review of Literature. J. Chestnut.—p. 323.
Some Problems in Economics of Medical Care. H. H. Shoulders. —p. 340.
*Single Massive Doses of Penicillin in Surgical Infections. B. J. Golden. —p. 344.
Proposed Federal Legislation Affecting Practice of Medicine. C. Revercomb.—p. 346.

Endemic Typhus.—Chestnut reports observations on 24 cases of endemic typhus observed in the Nashville General Hospital over a six months period. There were 16 men and 8 women, 14 of whom were white and 10 were Negroes. Cutaneous manifestations were observed in 15 patients. The rash appeared between the fourth and seventh days of the disease. It usually began fading from four to six days after its first appearance. It was of maculopapular type, varying in color from rose-red to dark red, and in one instance it was of a copper-like color. One of the patients, a woman aged 71, died; in the others convalescence was rapid and uneventful. The Weil-Felix reaction with Bacillus proteus X-19 was positive in all cases; the initial reaction was negative in 6 cases, but 14 revealed an increase in the titer as the disease progressed. There is no specific treatment for this rickettsial disease, although para-aminobenzoic acid has been used with good success.

Massive Dose of Penicillin in Surgical Infections.—Golden stresses the following points as worthy of note in the use of penicillin: (1) penicillin kills bacteria on contact; (2) large doses are relatively nontoxic and (3) bacteria may become penicillin fast very rapidly. With these points in mind, he decided to use single massive doses in surgical infections. He reports 8 cases in which he applied a large dose, usually 500,000 units, locally. The conditions treated included perforated appendix with peritonitis, cesarean operations, stab wounds and perforated gastric ulcer. He concluded that the massive dose by direct contact is of greater value than the massive dose by divided systemic administration. Many organisms which at present are considered insensitive to the drug either are destroyed or rendered nonpathogenic by penicillin when used in the manner described. It would appear that penicillin given intraabdominally destroys colon bacilli.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted. Single case reports and trials of new drugs are usually omitted.

Lancet, London

2:457-496 (Sept. 27) 1947

Ganglia in Communicating Rami of Cervical Sympathetic Trunk. T. Skoog.—p. 457.
Nutritional Value of Diets Eaten by Old People in London. M. Pyke, R. Harrison, Susan Holmes and Kathleen Chamberlain.—p. 461.
The Walking Calliper. J. Charnley.—p. 464.
Irregular Response to Liver Extract in Pernicious Anemia. J. F. Wilkinson and M. C. G. Israels.—p. 468.
Treatment of Acute Appendicitis. Tina Gray.—p. 469.

2:497-530 (Oct. 4) 1947

*British Anti-Lewisite: Its Use and Therapeutic Value in Arsenical Intoxications. R. A. Peters and others.—p. 497.
Kidney Function in Diabetes Insipidus. A. Greiner and L. Podhradszky.—p. 498.
Amidone (Miadone) as an Obstetric Analgesic: Trial in 62 Cases. F. Prescott and Shila G. Ransom.—p. 501.
Potassium Chlorate Poisoning: Report of Case. Susanna Gordon and J. A. H. Brown.—p. 503.
*Penicillin in 1 Per Cent Beeswax-Arachis Oil. H. Brindle, R. W. Fairbrother and F. B. Jackson.—p. 505.
Alopecia Areata Treated with Thorium-X. P. J. Feeny.—p. 506.
Opsoclonia: Rare Ocular Sign in Polioencephalitis. D. E. Marmion and J. Sandilands.—p. 508.
Revolt From Bedpan and Enema. G. Bohmansson and H. Malmros.—p. 509.

British Anti-Lewisite (BAL) in Arsenic Poisoning.—The trial with BAL (2,3-dimercaptopropanol) reported by Peters and his associates of the BAL Conference, Medical Research Council, was based on results obtained in 44 patients with severe and widespread arsenical dermatitis of the acute exfoliative type. The ampules of 2 3-dimercaptopropanol contained 5 per cent BAL in peanut oil and benzyl benzoate; they were nitrogen filled and were sterilized by heating for one hour at 170 C. The drug was given by deep intramuscular injection into the thigh or gluteal region. On the first day four injections of 2 cc. of 5 per cent BAL were given at four hour intervals; on the second, third and fourth days 2 cc. was given twice a day and on the fifth and sixth days 2 cc. was given once daily. Of the 44 patients studied 31 were benefited by the treatment. Healing was obtained in an average of twenty-one days. The earliest sign of response was subsidence of the edema.

Penicillin in Beeswax and Peanut Oil.—Brindle and his associates discuss the pharmacologic aspects of penicillin preparations. Whereas the British Pharmacopeia's formula uses the calcium salt of penicillin to the equivalent of 125,000 units per cubic centimeter in a vehicle of beeswax and peanut oil, various authorities have recommended that the strength be increased to 300,000 units per cubic centimeter. Trials of this preparation have been made by two methods: (1) assays of the blood level at intervals after intramuscular injection and (2) clinical trials in 28 cases of acute gonorrhea. The injections have usually been made into the gluteal muscles. The authors observed that effective blood penicillin levels were maintained and satisfactory clinical results were obtained with this preparation. It is fluid at room temperature and can be injected without difficulty.

Medical Journal of Australia, Sydney

2:285-320 (Sept. 6) 1947

Development of Obstetrics and Gynecology. W. F. Shaw.—p. 285.
*Some Clinical Aspects of Carbon Monoxide Poisoning. A. B. Corkill.—p. 289.
Penicillin in Abdominal Surgery, with Special Reference to Its Intraperitoneal Use. V. M. Coppleson.—p. 292.

Carbon Monoxide Poisoning.—According to Corkill carbon monoxide is nontoxic, but owing to its decided affinity for hemoglobin it precludes oxygen from entering into combination with this pigment. As a result of cerebral anoxia, the intellect, behavior and consciousness of the person are affected. Maniacal shouting, extreme restlessness and struggling may occur. Since the basal ganglions are affected, there may be hypertonia, increased or absent deep reflexes, clonus and bilateral Babinski responses. Cerebral edema with consequent rise in the pressure of the cerebrospinal fluid is another characteristic. The troublesome headache which is associated with mild poisoning or persists after recovery from severe poisoning is attributable to cerebral edema. The diagnosis of carbon monoxide poisoning in most cases is obvious from the history. With a patient in deep coma it may be possible to establish the diagnosis by demonstrating the pink color of diluted blood. In carbon monoxide poisoning the temperature of the body falls; hence, appropriate steps should be taken to avoid this. A patient recovering from carbon monoxide poisoning should not be allowed to walk about. Carboxyhemoglobin alters the dissociation curve of oxyhemoglobin, so that the latter cannot supply oxygen to the tissues at the normal rate. While the patient is at rest the oxygen supply might be sufficient, but any extra demand cannot be met. "Carbogen," which is 95 per cent oxygen with 5 per cent carbon monoxide, has been used and in addition following adequate "carbogen" therapy, if there still persist signs of increased intracranial pressure, 60 to 80 cc. of a 15 per cent sodium chloride solution should be given intravenously. Transfusion is dangerous and out of place. Occasionally cases are encountered in which both venesection and transfusion have been performed, the idea presumably being to replace blood containing carboxyhemoglobin with normal blood. A consideration of the rapid elimination of carbon monoxide under the influence of "carbogen" should suffice to discount the value of the former treatment. It is doubtful that drugs have a beneficial effect, except caffeine that is injected intravenously.

Acta Cardiologica, Brussels

2:113-200 (No. 2) 1947. **Partial Index**

Similarity of Circulatory Insufficiency in Shock with Diminished or Normal Amount of Blood. C. J. Wiggers.—p. 113.
*Problems Presented by Polyps of Left Auricle. I. Mahaim.—p. 136.
Study of Unipolar Electrocardiographic Derivations of Members. F. van Dooren and N. Boyadjian.—p. 144.
Various Aspects of Disturbances of Intraventricular Conduction. M. Segers, M. Vastesaeger and H. Denolin.—p. 166.

Polyp of Left Auricle.—Mahaim reports the case of a man, aged 49, with a polyp in the left auricle. A polyp is a tumor which grows and gradually fills the cardiac chamber in which it develops; it finally occludes the mitral orifice. It is of thrombotic or myxomatous origin. Clinical examination reveals transitory signs of mitral stenosis, in that the murmur appears and disappears from day to day or according to the patient's posture. Another characteristic of a polyp is that it discharges small particles of tissue into the blood stream and thereby produces small embolisms in the peripheral arteries. The surgical removal of such an embolus and its microscopic examination make possible a definite diagnosis of polyp of the left auricle. The only effective treatment of auricular polyp is its surgical removal. In view of the tremendous progress achieved in cardiac surgery during recent years, the surgical removal of auricular polyps can be considered with optimism.

Acta Tuberculosea Scandinavica, Copenhagen

21:1-240 (No. 1-3) 1947. **Partial Index**

*Epidemic of Tuberculosis in a State School, with Observation Period of About Three Years. T. V. Hyge.—p. 1.
Tuberculosis Epidemic of Faroe Islands. A. Poulsen.—p. 58.
Is There Any Risk of Infection from Gastric Lavage Positives? I. Bluhm.—p. 70.
Connection Between Tuberculin Allergy and Tubercle Bacillus Allergy: Clinical and Experimental Investigations. O. K. Thomassen.—p. 87.
Purified Tuberculin, Its Preparation and Properties. P. Lind.—p. 111.
*Deep Swab Culture, New Method for Cultural Demonstration of Tubercle Bacilli by Laryngeal Swabbing. L. Sula.—p. 160.
Unorthodox Artificial Pneumothorax: Clinical Study on Collapse Therapy. E. G. W. Hoffstaedt, with radiologic interpretations by H. Miller.—p. 169.
Permanent Results of Apical Thoracoplasty in Treatment of Lung Tuberculosis. F. Hagn-Meincke.—p. 190.

Epidemic of Tuberculosis in State School.—Hyge reports on an epidemic outbreak of tuberculosis which occurred in an explosive manner in a state school for young girls about five weeks after the obligatory annual examination for tuberculosis had been carried out. Of 368 pupils between the ages of 12 and 18 years who submitted to this obligatory examination, 105 were tuberculin negative; 133 were BCG vaccinated and tuberculin positive, and 130 were tuberculin positive (Mantoux's test). Of the 105 tuberculin-negative pupils, 94 of whom were exposed to the infection, 70 became tuberculin positive, i. e., 74.5 per cent.

In 6 of these progressive pulmonary tuberculosis developed. In 1 of them death resulted from generalized tuberculosis. Among the 133 BCG-vaccinated pupils, 106 of whom had been exposed to the infection, pulmonary tuberculosis was manifested in 2 (i. e. 1.9 per cent) about one year after the infection. Only 1 of the BCG-vaccinated and tuberculin-positive pupils had become tuberculin negative again, and she also had pulmonary tuberculosis about one year after the infection. Primary disease was not demonstrated in the infected BCG-vaccinated pupils. Among the 130 tuberculin-positive pupils (Mantoux's test) 105 of whom were exposed to the infection, pulmonary tuberculosis occurred in 4. Only 2 of these could be looked on as instances of exogenous reinfection, i. e. 1.9 per cent. The source of infection was a female teacher in whom an active lesion of pulmonary tuberculosis had not been demonstrated before the epidemic outbreak and after that was revealed only by tomography and gastric lavage examination. The infection was transmitted in some small classrooms in the basement of the school, particularly in a blacked-out room which also served as an air raid shelter and was lacking in ventilation and daylight. This epidemic demonstrated the significance of the immunity acquired through an earlier spontaneous tuberculous infection as well as that acquired through BCG vaccination. In spite of the considerable protection against tuberculosis offered by the immunity, it may suffer a breakdown on exposure to a particularly virulent infection. BCG vaccination should be employed at any rate before the occurrence of puberty.

Deep Swab Culture.—According to Sula the chance of losing tubercle bacilli by washing the laryngeal swab of patients with tuberculosis may be limited to a minimum as follows: first a tube with fluid medium and then two tubes with egg medium are inoculated with the swab. The apparently completely utilized swab is not thrown away but is immersed in another tube with fluid medium, in which it remains during the incubation of the culture, i. e. for three to four weeks. For this last culture the term "deep swab culture" has been suggested. The employment of the fluid medium makes it possible to utilize fully the cough droplets on the swab, because after the inoculation of the egg medium the entire swab is immersed in the fluid culture. Depending on the material, the positive cultural results from 1,985 laryngeal swabs varied between 13.5 per cent and 28.8 per cent among patients whose sputum on direct microscopic examination was observed to be negative. The deep swab culture has given positive results in cases with two negative egg medium cultures and one negative fluid culture.

Deutsche medizinische Wochenschrift, Stuttgart

72:465-496 (Sept. 5) 1947. **Partial Index**

Cavity Carcinoma. S. Graff.—p. 465.
Clinical Experiences on Penicillin Treatment of Gonorrhea. O. Grütz. —p. 467.
*Flight Sterility. F. Siegert.—p. 470.
*Chronic Forms of Epidemic Hepatitis with Regard to Their Clinical Symptomatology. H. Kalk.—p. 471.
*Cholecystopathies Following Epidemic Hepatitis. W. Stockinger.—p. 476.
Myocardial Impairment in Dysentery. H. Habs.—p. 477.
Five Day Fever, Louse Fever, Short Fever. R. Bieling.—p. 479.
Mistakes in Treatment of Syphilis. G. Mahn.—p. 486.

Flight Sterility.—Siegert comments on a report by Martins on the neurosympathetic reaction caused by severe psychic trauma, which by way of the diencephalon and the tuber cinereum elicits hormonal disturbance in the anterior lobe of the hypophysis. He thinks that "flight amenorrhea" is a suitable term for this psychogenic form of ovarian dysfunction. He reviews observations on a number of women between 25 and 30 years of age, who had experienced severe psychic shocks and repeated rape. The shock apparently had elicited amenorrhea, for they asked medical advice thinking that the rape might have resulted in conception. This, however, was not the case. That the women previously had not been sterile was indicated by the fact that they all had two or three children, between the ages of 2 and 10 years. The author regards the "flight amenorrhea" and "flight sterility" as nature's protection against procreation under unnatural and forced conditions.

Chronic Forms of Epidemic Hepatitis.—Anatomic studies by means of laparoscopy and of aimed hepatic puncture convinced Kalk that acute epidemic hepatitis can be designated as the large red liver. This form may develop into the large white liver, then the enlarged varicolored, then the variegated humpy liver and into hepatic cirrhosis. On the other hand, acute hepatitis may develop by way of acute (yellow) dystrophy of the liver into the coarse nodular atrophy which has been designated as potato liver. Acquired hemolytic icterus may result from epidemic hepatitis. Only the enlarged varicolored liver and the varicolored humpy liver can be regarded as chronic epidemic hepatitis in the strict sense of that term. The enlarged white liver is only a transitional stage to these chronic forms, and atrophic cirrhosis and coarse nodular atrophy and perhaps acquired hemolytic icterus may develop not only as sequels of epidemic hepatitis but probably also from other causes. This is definitely the case with cirrhosis, which is the reaction of a parenchymatous organ to prolonged inflammatory irritation. In a table the author surveys the differential diagnostic characteristics of posthepatitic diseases. This table lists under clinical signs chiefly those obtained by palpation. It also lists the results of the bilirubin determination in the serum, the erythrocyte sedimentation test, Gross's test (titration of serum with Hayem's solution), Takata's test in the modification by Mancke and Sommer and the blood sugar curve following injection of 10 units of insulin, and gives the various data obtained by duodenal aspiration. At his hospital vitamins B and C (ascorbic acid) and injections of lactoflavin and nicotinic acid have failed in serious cases. In the milder cases it is not certain whether improvement resulted from treatment or was spontaneous. Massive doses of extracts of the adrenal cortex seemed to be effective in the severe cases of acute hepatitis with transition into acute yellow atrophy, whereas in serious cases of enlarged varicolored liver they proved ineffective. Insulin-dextrose therapy is regarded as useless.

Cholecystopathies After Epidemic Hepatitis.—Among 200 men with a history of hepatitis, Stockinger found 78 with symptoms indicative of disturbances of the gallbladder. The results of palpation, duodenal aspiration and cholecystography corroborated the existence of cholecystic disease. The fact that the majority of these men with cholecystopathies belonged to the age group 25 to 30 years indicated a causal relation to the hepatitis. Stockinger thought that an allergic mode of onset was indicated by the fact that the disease of the gallbladder usually appeared from two to four months after the onset of hepatitis. This abacterial cholecystopathy which develops on an allergic basis may, however, provide the milieu for the development of a secondary bacterial infection and thus give rise to a chronic relapsing infectious cholecystitis.

Nordisk Medicin, Gothenburg

35:1611-1650 (Aug. 1) 1947. **Partial Index**

Latent Viruses and Their Relation to Infection. F. L. Horsfall Jr. —p. 1611.
Penicillin Treatment of Acute Pleural Empyema. Advantages, Disadvantages, Lines of Guidance. S. Brechling and J. L. Hansen.—p. 1618.

Hospitalstidende

*Retropubic Prostatectomy According to Millin. P. Morville.—p. 1623.
After-Examination of 103 Cases of Cancer with Reference to Evaluation of Preoperative and Postoperative Roentgen Treatment. M. Andreasen. —p. 1626.
Intake of Foreign Bodies by Psychopathic Patients. J. Sachs.—p. 1628.
Osteosynthesis According to Magnus. H. Haldbo.—p. 1630.

Finska Läkaresällskapets Handlingar

Rupture of Urinary Bladder. R. Jäfs.—p. 1633.

Hygiea

Sulfathiazole in Treatment of Infected Abortions. Rolf Fåhraeus. —p. 1641.

Retropubic Prostatectomy According to Millin.—Morville has used this method in 20 patients and finds that the method offers a safe and easy extravesical approach to the prostate, and easy enucleation. The operative field is in full view,

so that possible adherent adenomas or cancer tissue, necrotic tissue shreds and prostatic calculi can be seen and removed and bleeding vessels readily ligated. Suture of the prostatic bed above the inserted catheter avoids the creation of the dead space, the frequent site of secondary hemorrhage or grave postoperative infection. Neither sphincter is injured. Subjectively, the patient's condition is better than after the classic method, and the after-treatment is far less inconvenient for both patient and nurse.

Revista de la Asociación Méd. Argentina, Buenos Aires

61:501-554 (July 15-30) 1947. **Partial Index**

*Femoral Arteriovenous Aneurysm of Rare Characteristics. J. M. Jorge and L. Feldman.—p. 501.
*Prevention of Gonorrheal Conjunctivitis in Newborn. F. Páez Allende. —p. 514.

Arteriovenous Femoral Aneurysm.—The author believes this to be the fifth case to be reported in the literature. The patient had received a knife wound to his thigh at the age of 8 years. At the age of 13 a tumor was noted below the scar. The patient was a cowboy and horse tamer. At 17 the superficial veins of the calf became prominent, the leg cyanotic and the foot swollen. He did not have syphilis. A series of thirteen local sclerosing injections, at the age of 38, failed to obliterate the tumor. At 44 the leg and foot were cyanotic. The leg exhibited varicose veins. The temperature of the limb was higher than that of the other limb. The tumor near the scar was the size of a fetus's head, and pulsated visibly. Superficial palpation revealed a trill and auscultation and demonstrated a loud murmur. There was an enormous pelvic sac, arising from the external iliac vein, which acted as an accessory depot for the blood when the aneurysm was compressed in the course of the patient's work. The femoral sac was resected. The patient died from postoperative shock. Necropsy revealed that the pelvic aneurysm acted as a depot for the blood during the compression of the femoral aneurysm. This mechanism of adaptation between the aneurysm and the abdominopelvic sac explains the tolerance by the patient of his disease for so many years.

Prevention of Gonorrheal Conjunctivitis in Newborn.—The author contaminated the lower tarsal conjunctiva of volunteer adults with pus from the urethra of patients with gonorrheal urethritis. The pus on microscopic examination contained a large number of typical neisserian gonococci. Ten drops of a 10 per cent sulfathiazole solution was instilled into the eye immediately after its contamination. Six hours later five drops of a 5 per cent penicillin solution was applied. Gonorrheal conjunctivitis failed to develop in any of the cases. The author urges the employment of penicillin and sulfathiazole solutions in place of silver nitrate solution in the prevention of ophthalmia of the newborn.

Schweizerische medizinische Wochenschrift, Basel

77:967-1022 (Sept. 13) 1947. **Partial Index**

Changes in Panorama of Diseases in Sweden During Last Fifty Years. F. Henschen.—p. 968.
Present Status of Knowledge of Olfactory System of Brain. A. Brodal. —p. 971.
*Blood Transfusions in Treatment of Rheumatoid Arthritis. O. Appelqvist and Ö. Holsti.—p. 977.
Oxygen and Carbon Dioxide Content of Arterial Blood in Bronchial Asthma and Influence of Broncholytic Spray. F. Verzár and W. Vocgtli.—p. 980.
Psychoses Reslting from Abuse of Sleepiness Counteracting, Synthetic Amine Compounds. A. Harder.—p. 982.
Influence of Dihydroergotamine (DHE 45) on Psychomotor Excitation. B. Pritzker.—p. 985.
*First Results of Treatment of Tuberculosis with Streptomycin. M. Chauvet, Y. Gobat and H. Sulzer.—p. 989.

Blood Transfusions in Rheumatoid Arthritis.—Appelqvist and Holsti report 24 cases of rheumatoid arthritis, mostly severe, in 15 women between the ages of 20 and 59 and in 9 men between the ages of 29 and 50 years. Basic treatment consisted of constitutional rehabilitation, prevention of deformities and treatment of deformities. In addition two to thirteen weekly transfusions of blood were given. Results were favorable, although dramatic improvement was infrequent. The average decrease of the blood sedimentation rate was about 20 mm. in ten to eleven weeks. Pain, exudate and contraction were reduced to a somewhat greater extent than might have been expected from basic treatment alone. Blood transfusions may be given a fair trial in the form of a long series, in preference to and before resorting to gold therapy. Blood transfusions are recommended particularly for young and anemic patients in an early stage of rheumatoid arthritis.

Streptomycin in Tuberculosis.—Chauvet and his co-workers gave streptomycin to 30 patients with various forms of tuberculosis. One of 2 patients with acute miliary tuberculosis without meningitis made a clinical recovery of five and one half months' duration; the second is improved but still under treatment. Decisive improvement of the pulmonary dissemination resulted in 2 additional cases of acute miliary tuberculosis associated with tuberculous meningitis. However, the disease was fatal in 1 patient who, while moribund, was treated with streptomycin by the intraspinal route, although the meningitis was improved in the other. Two of 3 patients with tuberculous meningitis not associated with acute miliary tuberculosis made a clinical recovery of one and of five months' duration, while the third patient is still under treatment. Eleven patients with progressive pulmonary tuberculosis were treated by the intramuscular route; there was subjective improvement with increase in body weight and improved general condition in all cases with drop in temperature in 7 patients who were febrile. Four patients with acute laryngotracheobronchitis manifested immediate improvement. Diarrhea which persisted for two and one half months disappeared instantly in 1 patient. Two patients became free of bacilli. Roentgenologic examination revealed definite improvement in 5 cases and simultaneous progress and regression in 2 cases; 1 patient appeared worse. Five patients became worse within one to several weeks after treatment was discontinued. Encouraging results were obtained with local instillation of streptomycin in the tuberculous cavity of patients with Monaldi's drainage and likewise with intrapleural and intravesical treatment. Streptomycin was well tolerated except for intraspinal injections, which may be associated with severe risk but are indispensable in the treatment of tuberculous meningitis. The encouraging results in pulmonary tuberculosis do not warrant abandoning the classic methods of collapse therapy.

Wiener medizinische Wochenschrift, Vienna

97:381-404 (Sept. 6) 1947

Iron Bouillon, a Nutritive Culture Medium for Anaerobes. K. Berger. —p. 381.
Neuritic Manifestations as Primary Signal in Bone Syphilis. E. M. Klausberger.—p. 385.
*Treatment of Free Perforating Ulcers. A. Haeffner.—p. 388.
Modern Campaign Against Aerogenic Infections in Surgical Wards. J. Dischreit.—p. 390.
Method of Resection of Deeply Situated Ulcers of the Anterior Wall of Duodenum. A. Seidl.—p. 394.

Treatment of Free Perforating Ulcers.—Haeffner reports 318 cases of perforating ulcers, 10 of which were complicated by simultaneous severe gastric hemorrhage. In the 308 uncomplicated cases the ratio of duodenal to gastric ulcer was 9 to 1 and the ratio of men to women was 15 to 1. Thirteen patients did not undergo surgical operation. Of the remaining 295 patients, the opening was sutured in 197 (66.8 per cent); in 10 (3.4 per cent) with stenosis the closure was combined with gastroenterostomy; in 3 patients (1.1 per cent) Neumann's drainage was practiced but was ineffective, and primary resection was performed in 85 patients (28.7 per cent). Death occurred in 50 of the 197 patients in whom the ulcer was closed, and there were 4 fatal cases among the 85 patients with primary resection. Closure was done in 7 of the 10 patients in whom perforation of the ulcer was complicated by gastric hemorrhage, and 4 of them died. Primary resection was performed in 2 who survived, and longitudinal excision of the ulcus was done on 1 patient who died. Primary resection is urged in all cases of chronic ulcer within six hours of the perforation, provided that the general condition of the patient is satisfactory. Closure should be done in all cases and an additional gastroenterostomy in cases involving severe stenosis.

Book Notices

Peripheral Vascular Diseases (Angiology). By Saul S. Samuels, A.M., M.D., Chief of the Department of Peripheral Arterial Diseases, Stuyvesant Polyclinic Hospital, New York. Oxford Medical Outline Series. Second edition. Cloth. Price, $2.50. Pp. 85. Oxford University Press, 114 Fifth Ave., New York 11; Amen House, Warwick Sq., London, E. C. 4, 1947.

For those who like a compendium this outline of diagnosis and treatment of the peripheral vascular diseases should prove a conservative guide. Although one misses theory, variations in cases and the author's personal experience with them, one gets here, for application in general to the various types of peripheral vascular disease, the opinions of a physician who has long been a student, investigator and authority in this field. It is positive in its statements, as an outline must be, but an excellent bibliography at the end of each chapter gives the reader with curiosity an opportunity to become better acquainted with the work of others in this field. The general organization of the book is good but not consistent. The clinical picture is sometimes described under that heading, sometimes under "symptoms and objective symptoms" or just under "symptoms"; and in thromboangiitis obliterans it is omitted entirely. Since this outline is written for the general practitioner and general surgeon, it is understandable why skin temperature studies are not emphasized. But by the same token it is considered that undue emphasis is placed on the oscillometer which likewise requires skill and practice in the performance and interpretation of tests. One would like to see a statement to the effect that an evaluation of a given case is arrived at through the summation of the subjective symptoms, the objective observations and various tests. All tests used at present in the study of peripheral vascular diseases have definite drawbacks, and each has its school of supporters usually more than balanced by its detractors. The author's emphasis on the care to be used in dressings when dressings are indicated is important and if followed will in itself save feet and legs. The author's conservatism toward amputations and his plea that nature be allowed to self-demarcate and self-amputate toes is laudable. The reviewer notes with interest that a man of such broad experience expresses a general disapproval of the use of sympathectomy. This compendium will give the general practitioner or general surgeon practical facts which will aid him in the diagnosis and treatment of peripheral vascular diseases; and with that knowledge gained some physicians will undoubtedly want to pursue further this important subject.

Osteotomy of the Long Bones. By Henry Milch, M.D., Consulting Orthopedist, Maimonides Hospital, New York. Cloth. Price, $6.75. Pp. 294, with 181 illustrations. Charles C Thomas, Publisher, 301-327 East Lawrence Ave., Springfield, Ill., 1947.

This type of book does not lend itself readily to a review. The author sets out to present the mechanical aspects of osteotomy of the long bones, and his discussion is confined to the use of this one operative procedure. His stated object is to present the mode of action of each of the different types of osteotomy in terms of some general concepts. He found it necessary to demonstrate geometrically the effects of angulation of different degrees at different points on the shaft of the bone. He acknowledges that some readers may object to such geometrical basis on the grounds that it unduly burdens the reader. There are many reasons why mechanical precision is not always practicable in dealing with the deformities of the human skeleton. Nevertheless, the author has made an earnest effort to bring together theory and practice.

In this book are reviewed briefly the history of osteotomy and also the different types of osteotomy (lineal, torsional, transpositional and angulation). The rest of the book—about half—is devoted to the types of osteotomy used in lesions of the hip. One chapter, "The Post-Osteotomy Angle," is interesting and is deemed by the author to be extremely important. One must read this chapter to understand what the author is anxious to establish. It certainly is a rather complicated presentation for the average surgeon who is seeking help as to just where and how to do his osteotomy. Even to one accustomed to dealing with skeletal deformities, what might be called the "ground rules" in this particular chapter are none too clear, and careful and attentive reading is required to grasp the meaning. The author has included 44 reports of cases to illustrate his points. They could be abbreviated considerably without any decrease in value.

In spite of a few minor faults the book is a distinct contribution to the subject of osteotomy. The author is to be congratulated for doing as well as he has with a rather difficult subject, namely, the discussion of a specific operation which is applicable in a number of conditions. He has very creditably avoided the formidable danger of being led aside to discussions that would not be pertinent to osteotomy but which would be pertinent to the particular lesion that he is using as an example of the use of osteotomy. His other writings on the subject form the basis for this volume and will afford additional information to the reader who is sufficiently interested in the subject to consult them. The book is well designed and is printed on excellent gloss paper in a handsome type form. The orthopedic surgeon will be especially interested in this book and should have it in his library.

Diseases of the Gallbladder and Allied Structures: Diagnosis and Treatment. By Moses Behrend, M.D., F.A.C.S., F.I.C.S., Consulting Surgeon, Jewish Hospital and Mt. Sinai Hospital, Philadelphia. Foreword by Thomas A. Shallow, M.D., and Samuel D. Gross, Professor of Surgery, Jefferson Medical College, Philadelphia. Cloth. Price, $7. Pp. 290, with 110 illustrations. F. A. Davis Company, 1914-1916 Cherry St., Philadelphia 3, 1947.

This book is largely built around an excellent description of the anatomy of the region which carries the common duct, the hepatic artery and the portal vein. As every one knows, there is a great individual variation in these structures and in their relations one to another. Every young surgeon and some older ones who have to operate in this region will be grateful to Dr. Behrend for his many anatomic illustrations based on experience gained through years of dissections and operations.

There is much more in the book on the surgical treatment of gallbladder disease, on its complications and postoperative difficulties and also on surgical diseases of the pancreas.

Visible Speech. By Ralph K. Potter, Director of Transmission Research, Bell Telephone Laboratories, George A. Kopp, Associate Professor of Speech in the College of Literature, Arts and Sciences at the University of Michigan, Ann Arbor, and Harriet C. Green, Assistant Professor of Special Education at the Michigan State Normal College, Ypsilanti. Cloth. Price, $4.75. Pp. 441, with illustrations. D. Van Nostrand Co., Ltd., 250 Fourth Ave., New York 3, 1947.

In this volume is described a development of some of the members of the Bell Telephone Laboratories for recording on a movable screen temporary visible patterns produced by speech sounds. At present this idea is more experimental than practical, but further research in the field seems justified.

The authors describe the apparatus for the portrayal of intensity-frequency-time analysis of speech and tell how to display the results of the analysis to the eye. The apparatus for recording speech patterns is somewhat complicated, but the end result is of interest to those physicians and lay specialists who wish to aid the hard of hearing to understand speech or to improve the quality of speech marred by defects.

This method might be used in the future to train the hard of hearing to "see" speech. Thus persons who are hard of hearing may converse with hearing individuals by the spoken word.

The volume is of particular interest to the otologist and the speech correctionist and also to those lay persons interested in improving the lot of the hard of hearing and the deaf. The research worker and the technician will also be interested in the volume from a scientific point of view.

Estimation of the Vitamins. Edited by W. J. Dann and G. Howard Satterfield. Volume XII, Biological Symposia: A Series of Volumes Devoted to Current Symposia in the Field of Biology. Edited by Jaques Cattell. Cloth. Price, $6.50. Pp. 531, with illustrations. The Ronald Press Co., 15 E. 26th St., New York 10, 1947.

This is one of a series of volumes devoted to current symposiums in the field of biology. It is primarily of interest to chemists and others who have reason to want to know of the laboratory estimation of vitamins.

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

DIARRHEAS OF INFANCY

To the Editor:—**Please outline fluid administration, amount, route of administration and type of fluids, in both severe and moderately severe diarrheas of infancy. Then, how would you gradually introduce oral feedings and what would you use?**

M.D., Brooklyn.

ANSWER.—No set rule can be laid down for the treatment of diarrheas of infancy, as obviously the etiologic basis of each case must be considered. The moderately severe diarrheas which are not of specific origin, e.g., bacillary, can at times be controlled by stopping all food for twenty-four to thirty-six hours and allowing only water, and 2 to 3 ounces (60 to 90 cc.) of unsweetened tea every three hours. After this the infant, if breast fed, may be allowed at breast for five minutes after each administration of tea, and then the amount of tea gradually reduced and the time at breast increased until such a time as the infant is on a normal schedule. For artificially fed infants, after a twenty-four to thirty-six hour starvation period skimmed lactic acid milk may be used, giving about one-half the amount of formula that the baby normally gets at each feeding; the remainder of the fluid requirements may be met with tea or water. After a twenty-four hour trial with this routine the regular formula may be tried.

Severe diarrheas have to be treated more vigorously, and parenteral fluids must be given to restore fluid and electrolyte balance. In general 2½ to 3 ounces (75 to 90 cc.) of fluid per pound of body weight per twenty-four hours will be needed. This can be given by vein or subcutaneously. Prior to starting treatment, blood should be drawn for determination of the carbon dioxide content, hemoglobin concentration and plasma protein levels.

The types of fluids used will vary with each case, but an average distribution as suggested in the Mitchell-Nelson textbook of pediatrics is as follows: 2 Gm. of amino acids per pound of body weight per day, which can be given as a 5 per cent solution of amino acid in 5 per cent dextrose. The remainder of the fluids can be given as 5 per cent dextrose in isotonic sodium chloride solution; however, administration of too much sodium chloride must be avoided to prevent edema. About 1 Gm. of sodium chloride is needed per day in infancy. If the carbon dioxide combining power is under 40 volumes per cent, means to combat acidosis should be carried out, and this can be done by the use of sodium bicarbonate: 1 Gm. of sodium bicarbonate per kilogram of body weight will increase the carbon dioxide combining power by 38 volumes per cent.

Darrow, who has shown that there is a loss of potassium in infant diarrheas, advocates the use of a solution composed of potassium chloride 2 Gm., sodium chloride 3 Gm., molar sodium lacate 40 cc. and water 710 cc.; 80 to 100 cc. of the preceding solution per kilogram of body weight is given by vein or subcutaneously after the initial hydration has been completed in the first twenty-four hours. Smaller amounts, from 20 to 50 cc. per kilogram, are given after the first twenty-four hours. This solution must be used with caution, as it may cause potassium poisoning.

At times the use of plasma will be indicated.

Oral fluids should be limited to water and unsweetened tea, and once the diarrhea has subsided a regimen similar to that given for moderate diarrheas may be carried out.

Vitamin B and ascorbic acid should be continued, parenterally if necessary; vitamin D can be omitted during the acute episode.

Some physicians advocate the use of sulfonamide preparations, 1 to 1½ grains (0.06 to 0.09 Gm.) per pound of body weight per twenty-four hours.

PAINFUL MENSTRUATION AND ORGASM

To the Editor:—**What can be done for a woman, aged 32, who complains of painful and scanty menstruation, who has normal libido but is not able to have an orgasm. The physical findings are normal as far as can be discovered.**

M.D., Pennsylvania.

ANSWER.—In the presence of apparently normal pelvic organs, nothing need be done about the scanty menstruation. The pain associated with menstruation is, of course, not always easy to overcome. An effort may be made to prevent dysmenorrhea by suppressing ovulation. The simplest procedure is for the patient to take a 1 mg. tablet of diethylstilbestrol every night for sixteen nights beginning the first night of menstruation. This schedule is for women who menstruate every twenty-eight to thirty days. If the menstrual interval is longer, the diethylstilbestrol should be taken for a correspondingly longer number of days. This therapy sometimes produces menstrual irregularities, so that it should not be used for more than three months at a time. If this therapy does not help, one must rely on the customary simple pain relievers.

Some psychic element is present in most cases of dysmenorrhea is which no physical cause can be found, and in the case cited the psyche undoubtedly plays a role in the absence of an orgasm. Nearly all women who have normal libido can be made to have an orgasm provided the male uses the proper technic and, more important, provided the woman really loves her consort. In some cases libido can be stimulated and orgasms aided by the use of testosterone propionate. The usual dose for this purpose is 25 mg. hypodermically three times a week for four weeks. However, there is some danger of virilism from the use of 300 mg. of testosterone propionate.

GENERALIZED CUTANEOUS MONILIASIS

To the Editor—**What is the best treatment of generalized cutaneous eczematoid moniliasis and onychia stemming from the initial lesion of twenty years ago? The patient is a moderately obese housewife, aged 65, who has been and is being digitalized for auricular fibrillation and failure of thirteen years' duration. The patient says that the lesions have improved on two previous occasions: (1) twenty years ago another physician put the patient on a diet for being overweight, and the lesions on her left hand cleared up. On regaining the lost weight the lesions reappeared. (2) Six years ago a physician recommended roentgen therapy for the intertrigenous area of the left axillary region. This healed after six weeks' therapy only to recur shortly thereafter. Apparently, at no time in the past was the correct diagnosis made. Would iodides be contraindicated?**

M.D., New Jersey.

ANSWER.—The moniliases form a group of infections which have been known by different names but have in the last few years been brought together under the title moniliasis. Their common denominator is the pathogenic agent, a yeast organism. Thus thrush, certain intertrigos, erosio interdigitalis saccharomycetica, perlèche, certain paronychias and onychias belong to this group. They almost always begin in folds and usually remain there. Occasionally the disease may become generalized; rarely, it may become systemic, and if so the prognosis is grave. The relation of seborrhea and seborrheic eczemas, at least of some kinds, and the moniliases has been debated.

Cornbleet found no glucose in the sweat of these subjects, though as a group they show diminished sugar tolerance as indicated by their blood glucose curves. Urbach considered that he had evidence to the effect that such patients accumulate undue quantities of sugar in the skin and claimed good therapeutic results from restricted carbohydrate intakes. Pillsbury found that high feedings of carbohydrate predisposed experimental animals to pyogenic infections. He associated this phenomenon with increased cutaneous hydration. It might be well to study this woman's sugar tolerance. At any rate, it would do no harm to restrict her carbohydrates and reduce her weight.

Reservoirs for yeast organisms should be hunted in the gastrointestinal tract, the respiratory passages and the genital tract. It may be better to keep the parts dry rather than to use wet dressings, such as potassium permanganate solution. In cases in which the dermatitis is acute in nature, however, it is well to begin with wet dressings until this phase abates.

Antibiotics are not useful in the ordinary superficial fungous infections of the skin. However, in some cases there may be a secondary pyogenic factor. In such instances the use of penicillin ointment or a sulfonamide ointment or the administration of these agents by mouth might be useful. Their action should be watched closely, however, especially if they are applied to the skin. Too often they induce allergic manifestations, sometimes serious ones and even death. Methylrosaniline chloride (gentian violet) in 1 to 2 per cent aqueous solution is an excellent remedy for localized yeast infections. However, its use in these widespread varieties has not been attended with notable success. Sometimes by continued use of the gentian violet solution the skin becomes irritated, and the concentration of the solution needs to be reduced. The use of the vitamin B complex factors is sometimes worth while. The skin should be kept as dry as possible. Sometimes this may be aided by the use of a powder bath. Forty per cent sulfur ointment in petrolatum may be tried cautiously on a small area before applying it to larger ones. Sometimes a nonspecific agent, such as a milk preparation given intramuscularly, is beneficial and increases the effectiveness of adjuvant measures.

JOURNALS ABSTRACTED IN THE CURRENT MEDICAL LITERATURE DEPARTMENT, SEPTEMBER—DECEMBER 1947

Titles have been listed or abstracts made of important articles in the following journals in the Current Literature Department of THE JOURNAL during the past four months. Any of the journals, except those starred, will be lent by THE JOURNAL to subscribers in continental United States and Canada and to members of the American Medical Association for a period not exceeding three days. Three journals may be borrowed at a time. No journals are available prior to 1936. Requests for periodicals should be addressed to the Library of the American Medical Association and should be accompanied by stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Thus most of these journals are accessible to the general practitioner.

Acta cardiologica. Brussels.
Acta chirurgica Scandinavica. Stockholm.
Acta dermato-venereologica. Stockholm.
Acta medica scandinavica. Stockholm.
Acta obstetricia et gynecologica Scandinavica. Stockholm.
Acta radiologica. Stockholm.
Acta tuberculosea Scandinavica. Copenhagen.
American Heart Journal. St. Louis.
American Journal of Clinical Pathology. Baltimore.
American Journal of Digestive Diseases. Fort Wayne, Ind.
*American Journal of Diseases of Children. A. M. A., Chicago.
American Journal of Hygiene. Baltimore.
American Journal of the Medical Sciences. Philadelphia.
American Journal of Medicine. New York.
American Journal of Obstetrics and Gynecology. St. Louis.
American Journal of Ophthalmology. Cincinnati.
American Journal of Orthopsychiatry. New York.
American Journal of Pathology. Ann Arbor, Mich.
American Journal of Physiology. Baltimore.
American Journal of Psychiatry. New York.
American Journal of Public Health. New York.
American Journal of Roentgenol. and Radium Therapy. Springfield, Ill.
American Journal of Surgery. New York.
American Journal of Syphilis, Gonor. and Venereal Diseases. St. Louis.
American Journal of Tropical Medicine. Baltimore.
American Practitioner. Philadelphia.
American Review of Soviet Medicine. New York.
American Review of Tuberculosis. New York.
Anales de la Cátedra de patología y clínica de la tuberculosis. Buenos Aires.
Anesthesiology. New York.
Annales chirurgiae et gynaecologiae Fenniae. Helsinki.
Annales medicinae internae Fenniae. Helsinki.
Annales d'oto-laryngologie. Paris.
Annales paediatrici. Basel.
Annali di radiologia diagnostica. Bologna.
Annals of Allergy. Minneapolis.
Annals of Internal Medicine. Lancaster, Pa.
Annals of Otology, Rhinology and Laryngology. St. Louis.
Annals of the Rheumatic Diseases. London.
Annals of Surgery. Philadelphia.
Annals of Tropical Medicine. Liverpool.
Annals of Western Medicine and Surgery. Los Angeles.
*Archives of Dermatology and Syphilology. A. M. A., Chicago.
Archives of Diseases in Childhood. London.
*Archives of Internal Medicine. A. M. A., Chicago.
Archives des maladies de l'appareil digestif. Paris.
Archives des maladies professionnelles, de médecine du travail et de sécurité sociale. Paris.
*Archives of Neurology and Psychiatry. A. M. A., Chicago.
*Archives of Ophthalmology. A. M. A., Chicago.
*Archives of Otolaryngology. A. M. A., Chicago.
*Archives of Pathology. A. M. A., Chicago.
Archives of Physical Medicine. Chicago.
*Archives of Surgery. A. M. A., Chicago.
Archivio di Antropologia criminale, psichiatria e medicina legale. Turin.
Archivos del Instituto de cardiología de México, Mexico, D. F.
Archivos de medicina infantil. Havana.
Archivos de pediatría del Uruguay. Montevideo.
Archivos uruguayos de medicina, cirugía y especialidades. Montevideo.
Arizona Medicine. Phoenix.
Australian Journal Experimental Biology and Medical Science. Adelaide.
Australian and New Zealand Journal of Surgery. Sydney.
Belgisch Tijdschrift voor Geneeskunde. Louvain.
Boletín del ateneo médico de Lima. Lima.
Blood. New York.
Brain. London.
British Heart Journal. London.
British Journal of Dermatology and Syphilis. London.
British Journal of Experimental Pathology. London.
British Journal of Industrial Medicine. London.
British Journal of Ophthalmology. London.
British Journal of Radiology. London.
British Journal of Surgery. Bristol.
British Journal of Tuberculosis. London.
British Journal of Urology. London.
British Medical Journal. London.
Bruxelles-médical. Brussels.
Bulletin of the Johns Hopkins Hospital. Baltimore.
Bulletin of the Los Angeles Neurological Society. Los Angeles.
Bulletin of the New York Academy of Medicine. New York.
Bulletin of the U. S. Army Medical Department. Washington, D. C.
California Medicine. San Francisco.
Canadian Journal Public Health. Toronto.
Canadian Medical Association Journal. Montreal.
Cancer Research. Baltimore.
Cardiologia. Basel.
Chinese Medical Journal. Washington, D. C.
Cincinnati Journal of Medicine. Cincinnati.
Connecticut State Medical Journal. Hartford.
Delaware State Medical Journal. Wilmington.
Dermatologica. Basel.
Deutsche medizinische Wochenschrift. Stuttgart.
Día médico. Buenos Aires.
Diseases of Chest. Chicago.
East African Medical Journal. Nairobi.
Edinburgh Medical Journal.
Endocrinology. Springfield, Ill.
Experimental Medicine and Surgery. Brooklyn.
Gaceta médica de México. Mexico, D. F.
Gastroenterologia. Basel.
Gastroenterology. Baltimore.
Gazzetta medica Italiana. Milan.
Geriatrics. Minneapolis.
Giornale di medicina militare. Rome.
Glasgow Medical Journal.
Hawaii Medical Journal. Honolulu.
Helvetica chirurgica acta. Basel.
Helvetica medica acta. Basel.
Helvetica paediatrica acta. Basel.
Illinois Medical Journal. Chicago.
Industrial Medicine. Chicago.
Irish Journal of Medical Science. Dublin.
Journal of Allergy. St. Louis.
Journal of the Arkansas Medical Society. Fort Smith.
Journal of Aviation Medicine. St. Paul.
Journal of Bacteriology. Baltimore.
Journal of Bone and Joint Surgery. Boston.
Journal of Clinical Endocrinology. Springfield, Ill.
Journal of Clinical Investigation. Boston.
Journal of Endocrinology. London.
Journal of Experimental Medicine. New York.
Journal of the Florida Medical Association. Jacksonville.
Journal of Gerontology. Springfield, Ill.
Journal of Hygiene. London.
Journal of Immunology. Baltimore.
Journal of the Indiana State Medical Association. Indianapolis.
Journal of Industrial Hygiene and Toxicology. Baltimore.
Journal of Infectious Diseases. Chicago.
Journal International de Chirurgie. Brussels.
Journal of International College of Surgeons. Chicago.
Journal of Investigative Dermatology. Baltimore.
Journal of the Iowa State Medical Society. Des Moines.
Journal of the Kansas Medical Society. Topeka.
Journal of Laboratory and Clinical Medicine. St. Louis.
Journal of the Maine Medical Association. Portland.
Journal of the Medical Association of the State of Alabama. Montgomery.
Journal of the Medical Association of Georgia. Atlanta.
Journal of the Medical Society of New Jersey. Trenton.
Journal of Mental Science. London.
Journal of the Michigan State Medical Society. Lansing.
Journal of the Missouri State Medical Association. St. Louis.
Journal of the Mount Sinai Hospital. New York.
Journal of the National Cancer Institute. Washington, D. C.
Journal National Malaria Society, Columbia, S. C.
Journal of Nervous and Mental Disease. New York.
Journal of Neurology, Neurosurgery and Psychiatry. London.
Journal of Neuropathology and Experimental Neurology. Baltimore.
Journal of Neurophysiology. Springfield, Ill.
Journal of Neurosurgery. Springfield, Ill.
Journal of Nutrition. Philadelphia.
Journal of Obstetrics and Gynaecology of the British Empire. Manchester.
Journal of the Oklahoma State Medical Association. Oklahoma City.
Journal of Pediatrics. St. Louis.
Journal of Pharmacology and Experimental Therapeutics. Baltimore.
Journal of the Philippine Medical Association. Manila.
Journal of Physiology. Cambridge.
Journal of the Royal Institute of Public Health and Hygiene. London.
Journal of the South Carolina Medical Association. Florence.
Journal of the Tennessee State Medical Association. Nashville.

*Cannot be lent.

Journal of Thoracic Surgery. St. Louis.
Journal of Tropical Medicine and Hygiene. London.
Journal of Urology. Baltimore
Journal-Lancet. Minneapolis.
Kentucky Medical Journal. Bowling Green.
Khirurgiya. Moscow.
Kuba. Havana.
Lancet. London.
Laryngoscope. St. Louis.
Lyon chirurgical. Paris.
Medical Annals of the District of Columbia. Washington.
Medical Journal of Australia. Sydney.
Medicina internazionale. Milan.
Medicina latina. Havana.
Military Surgeon. Washington, D. C.
Minerva chirurgica. Turin.
Minerva medica. Turin.
Minnesota Medicine. St. Paul.
Nebraska State Medical Journal. Lincoln.
Nederlandsch Tijdschrift voor Geneeskunde. Amsterdam.
New England Journal of Medicine. Boston.
New Orleans Medical and Surgical Journal. New Orleans.
New York State Journal of Medicine. New York.
New Zealand Medical Journal. Wellington.
Nordisk medicin. Gothenburg.
North Carolina Medical Journal. Winston-Salem.
Northwest Medicine. Seattle.
Occupational Medicine. A. M. A., Chicago.
Ohio State Medical Journal. Columbus.
Ophthalmologica. Basel.
Paris médical. Paris.
Pediatría de las Américas. Mexico, D. F.
Pediatria del medico pratico. Turin.
Pediatría prática. São Paulo.
Pennsylvania Medical Journal. Harrisburg.
Physiological Reviews. Baltimore.
Practitioner. London.
Praxis. Bern.
Presse médicale. Paris.
Proceedings of Royal Society of Medicine. London.
Proceedings of the Staff Meetings of the Mayo Clinic. Rochester, Minn.
Psychiatric Quarterly. Utica, N. Y.
Psychiatry. Washington, D. C.
Psychoanalytic Quarterly. Albany, N. Y.
Psychosomatic Medicine. Baltimore.
Public Health Reports. Washington, D. C.
Puerto Rico Journal of Public Health and Tropical Medicine. San Juan.
Quarterly Journal of Medicine. Oxford.
Quarterly Journal of Studies on Alcohol. New Haven, Conn.
Radiology. Syracuse, N. Y.
Review of Gastroenterology. New York.
Revista de la Asociacion médica argentina. Buenos Aires.
Revista clínica española. Madrid.
Revista española de pediatría. Zaragoza.
Revista medica del Ateneo Ramón y Cajal. Mexico, D. F.
Revista médica de Chile. Santiago.
Revista médica de Córdoba. Córdoba.
Revista de medicina y cirugía de la Habana. Havana.
Revista de medicina experimental. Lima.
Revue d'hématologie. Paris.
Revue de la tuberculose. Paris.
Rhode Island Medical Journal. Providence.
Rivista dell'istituto sieroterapico Italiano. Naples.
Rocky Mountain Medical Journal. Denver.
Sang. Paris.
Schweizerische medizinische Wochenschrift. Basel.
Schweizerische Zeitschrift für Tuberkulose. Basel.
Semaine des hôpitaux de Paris. Paris.
Semana médica. Buenos Aires.
South African Medical Journal. Cape Town.
Southern Medical Journal. Birmingham, Ala.
Southern Surgeon. Atlanta, Ga.
Surgery, Gynecology and Obstetrics. Chicago.
Surgery. St. Louis.
Texas State Journal of Medicine. Fort Worth.
Thorax. London.
Transactions of the Royal Society of Tropical Medicine and Hygiene. London.
Tubercle. London.
Union Medicale du Canada. Montreal.
United States Naval Medical Bulletin. Washington, D. C.
Urologic and Cutaneous Review. West Palm Beach, Fla.
Virginia Medical Monthly. Richmond.
Western Journal of Surgery, Obstetrics and Gynecology. Portland, Ore.
West Virginia Medical Journal. Charleston.
Wiener klinische Wochenschrift. Vienna.
Wiener medizinische Wochenschrift. Vienna.
Wisconsin Medical Journal. Madison.
Yale Journal of Biology and Medicine. New Haven.

SUBJECT INDEX

This is an index to all the reading matter in THE JOURNAL. In the Current Medical Literature Department only the articles which have been abstracted are indexed.

The letters used to explain in which department the matter indexed appears are as follows: "BI," Bureau of Investigation; "E," Editorial; "C," Correspondence; "OS," Organization Section; "ab," abstracts; the star (*) indicates an original article in THE JOURNAL.

This is a subject index and one should, therefore, look for the subject word, with the following exceptions: "Book Notices," "Deaths," "Medicolegal Abstracts" and "Societies" are indexed under these titles at the end of the letters "B," "D," "M," and "S." Matter pertaining to the Association is indexed under "American Medical Association." The name of the author, in brackets, follows the subject entry.

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Acad.—Academy	*Indust.—Industrial*
Am.—American	*Inst.—Institute*
A.—Association	*Internat.—International*
Coll.—College	*M.—Medical*
Commn.—Commission	*Med.—Medicine*
Comm.—Committee	*Nat.—National*
Conf.—Conference	*Pharm.—Pharmaceutical*
Cong.—Congress	*Phys.—Physicians*
Dist.—District	*Soc.—Society*
Div.—Division	*Surg.—Surgery*
Found.—Foundation	*Surgs.—Surgeons*
Hosp.—Hospital	*S.—Surgical*

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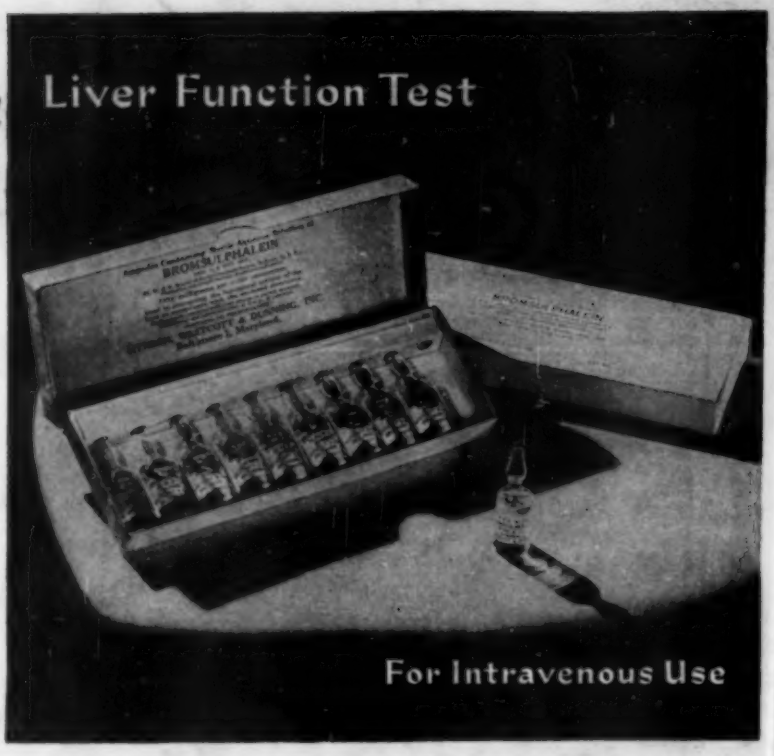

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